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PRELIMINARY CLINICAL OBSERVATIONS OF SERUM LIPASE ACTIVITY AS DETERMINED BY A COLORIMETRIC METHOD

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IN THE course of a study of the specificity of action of esterase and lipase on synthetic chromogenic substrates,[1] a method for colorimetrically measuring lipase activity in the presence of serum esterase was developed.[2] This method has several advantages over the titrimetric methods in current use[3]: (a) shortening of the incubation period to five hours; (b) simplification of the technical procedure by use of colorimetric measurement; and (c) avoidance of error, due to overlapping of esterase and lipase action on their respective substrates, by the use of the specific stimulating action of sodium taurocholate on pancreatic lipase.[1, 2, 4, 5]

Animal experiments have demonstrated fluctuations in serum lipase activity, as determined by this colorimetric method, which would be expected to occur following injection of Mecholyl and eserine,[4] following total pancreatectomy[6] and following the production of acute pancreatitis.[7] This suggested an evaluation of the test for the clinical diagnosis of pancreatic disease, since lipase, in contrast to amylase, is present in a significantly large amount only in pancreatic tissue.[1] The report that serum lipase was elevated for a longer time than serum amylase in pancreatic disease[8] suggested that this determination might be particularly useful in patients who are first seen relatively late, after the onset of severe symptoms. This seemed unlikely, however, following our observation of the low renal threshold for lipase in normal subjects,[9] as indicated by considerable quantities of lipase in the urine. A preliminary evaluation of the measurement of serum lipase activity with the new method was made in various clinical states reported in the following section.

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TABLE I. PANCREATITIS

HOSPITAL OR NUMBER	SEX	NONPROTEIN NITROGEN (MG. PER CENT)	BILIRUBIN (MG. PER CENT)	AMYLASE (UNITS PER 100 C.C.)	LIPASE (UNITS PER C.C.)	COLOR DENSITY IN KLETT UNITS		DIAGNOSIS AND BASIS FOR DIAGNOSIS
						WITHOUT TAUROCHOLATE	WITH TAUROCHOLATE	
VAH	M			595	3.5	510	600	Recurrent pancreatitis—history and pancreatic calcification by x-ray
BCH	M	23*	40†	8000	2.0	260	310	Acute pancreatitis—clinical picture
M7070	M	73	0.2	329	1.0	540	565	Acute pancreatitis—clinical picture, low calcium in serum
M7123	M			481	1.0	525	550	Acute pancreatitis—established at operation
Pratt					0.4	43	52	Recurrent pancreatitis—clinical picture
M7922	F			38	0	423	418	Chronic calcific pancreatitis—history and x-ray
M10222	M	37	2.5	249	0	475	228	Acute pancreatitis—clinical picture
M7667	F	54		1012	0	1000	820	Acute hemorrhagic pancreatitis—established at operation
M16872	F	60		537	0	717	538	Acute pancreatitis—established at operation
M17167	F		35†	419	0	501	255	Acute pancreatitis—clinical picture; subsequent laparotomy for common duct stone revealed pancreatitis residua
M17396	M			146	0	513	253	Subacute pancreatitis—indurated pancreas at operation
M16662	F		0.6	802	0	783	470	Acute pancreatitis—clinical picture
M19361	F		9†	871	0	488	425	Acute pancreatitis—clinical picture

*Blood urea nitrogen.
†Icteric index.

METHOD

The lipase activity of serum was determined in duplicate according to the procedure previously described.[2] Serum was usually obtained on the morning of the day the determination was made, although serum may be stored for two days at 4° C. without loss of lipase activity. Lipase activity is given in Tables I to V in units per cubic centimeter of serum. One unit of lipase was defined as that quantity of the enzyme, which in the presence of sodium taurocholate, is able to liberate 0.01 mg. of naphthol from beta naphthyl laurate in five hours at 37.5° C. in excess of that liberated by the esterase present in the same quantity of serum.[2] In the tables, the color density of the tube without taurocholate indicates the esterase activity, and the color density of the tube with taurocholate indicates both esterase and lipase activity when greater, or only esterase when the same or less. Lipase activity was calculated from the difference in color density of the two tubes by means of a calibration curve.[2] In the rare instance when the esterase activity of serum is extremely high (color density 1000), the inhibitory effect of taurocholate on esterase may mask the stimulation of a small amount of lipase. A correction for this phenomenon has not been made in the tables. Normal human serum was found to contain no lipase.[2] Hence the test may be considered to be positive when any lipase activity is found. Although only one lipase value is given in the tables, several determinations were made in many patients on consecutive days. At least one determination was made before the operation where indicated in the tables.

Other chemical determinations including nonprotein nitrogen or blood urea nitrogen, bilirubin or icteric index, thymol turbidity, and serum amylase,[10] when given in the tables, were taken from the hospital record.

RESULTS

For purposes of analysis, the clinical cases were grouped into several physiopathologic states in which increases in serum lipase activity might occur. These were: pancreatitis, carcinoma of the pancreas, common duct obstruction, hepatitis, gall bladder disease, renal insufficiency, diabetes mellitus, and other diseases without evidence of nitrogen retention. Protocol and laboratory data are given for patients in the first four categories (Tables I to IV) and results are summarized in Table V.

Pancreatitis (Table I).—In five of thirteen patients the serum contained lipase and increased amounts of amylase activity. Seven of the remaining cases with no serum lipase showed elevated amylase levels. The eighth case without detectable serum lipase was one of chronic calcific pancreatitis, and showed normal amylase activity as well. Five of these thirteen patients were explored at the time of admission, or shortly thereafter. No operative procedure was performed on the pancreas at the time of exploration. The one fatality occurred in a patient with a fulminating disease process who showed an elevated amylase with no serum lipase.

Carcinoma of the Pancreas (Table II).—The serum in one of six patients contained lipase. In this patient, the nonprotein nitrogen was 70 mg. per cent

TABLE II. CARCINOMA OF PANCREAS

HOSPITAL OR NUMBER	SEX	NONPROTEIN NITROGEN (MG. PER CENT)	BILIRUBIN (MG. PER CENT)	AMYLASE (UNITS PER 100 C.C.)	LIPASE (UNITS PER C.C.)	COLOR DENSITY IN KLETT UNITS		BASIS FOR DIAGNOSIS
						WITHOUT TAURO-CHOLATE	WITH TAURO-CHOLATE	
Pratt	F	70	25		0.4	168	175	Clinical picture and biopsy of skin metastasis
M9005	M	21		6	0	370	362	Operation
M8983	M	42	85†		0	405	360	Operation
M10057	M	25			0	375	230	Operation
BCH	M	10*	Normal	1600	0	420	248	Operation
M17139	F	32	Normal		0	382	231	Operation

*Blood urea nitrogen.
†Icteric index.

TABLE III. COMMON DUCT OBSTRUCTION

NUMBER	SEX	NONPROTEIN NITROGEN (MG. PER CENT)	BILIRUBIN (MG. PER CENT)	AMYLASE (UNITS PER 100 C.C.)	LIPASE (UNITS PER C.C.)	COLOR DENSITY IN KLETT UNITS		DIAGNOSIS AND BASIS FOR DIAGNOSIS
						WITHOUT TAURO-CHOLATE	WITH TAURO-CHOLATE	
M7460	M	42	5.5	51	16	205	615	Choledocholithiasis—operation
M9190	F	115	19	20	2.0	200	248	Choledocholithiasis—cholangiogram at operation
M9062	F	36	24		1.2	290	335	Obstructive jaundice—history of pain, no bile in stool, high alkaline phosphatase
M19690	F		2.3		0.8	282	297	Choledocholithiasis—operation
M9025	M		3.1		0.75	265	283	Choledocholithiasis—common duct obstructed by inflammatory reaction
M8455	F	20	1.8	136	0.06	150	153	Carcinoma of common duct—operation
M8820	F	27	3.5		0.06	185	187	Choledocholithiasis—operation
M9866	M	31	2.1	221	0.06	528	530	Choledocholithiasis—operation
M8580	M	22	18		0	145	145	Obstructive jaundice—biliary cirrhosis history
M7606	M	35	28*		0	460	440	Choledocholithiasis—operation
M11077	M	76	75*		0	410	350	Choledocholithiasis—operation
M16345	F	31	93*		0	255	199	Choledocholithiasis—operation
M14907	M	34	10.6	46	0	533	350	Carcinoma of common duct—operation
M15072	M	39	20	41	0	298	230	Carcinoma of gall bladder—operation
M19917	F		30.8		0	268	209	Clinical picture of choledocholithiasis, signed out against advice

*Icteric index.

(see Table II). Another patient had common duct obstruction as indicated by severe jaundice. A third patient had long-standing pancreatic duct obstruction as indicated by the marked dilatation of the duct at operation. Five of these patients were explored. The sixth, with a typical clinical picture and widespread metastases, had a positive skin biopsy.

Obstruction of the Common Duct (Table III).—The serum in eight of fifteen patients contained lipase. In three of these eight patients the serum activity was low. Although anatomic studies have indicated a high incidence of communication of the pancreatic duct with the common bile duct,[11] the cause of the frequent appearance of lipase in the blood in common duct obstruction is not clear.

Hepatitis (Table IV).—Lipase was not demonstrable in the serum of fifteen patients, thirteen with severe jaundice. Amylase determinations were not made. Four of five additional cases (included under other diseases) with cirrhosis of the liver and elevated bilirubin showed no serum lipase. The fifth patient with biliary cirrhosis, proved at previous laparotomy, had a persistent elevation of serum lipase for over fifteen months.

Gall Bladder Disease Without Common Duct Obstruction.—The serum in two of twenty patients contained lipase. One of the two patients had decreased renal function as evidenced by a blood nonprotein nitrogen level of 54 mg. per cent. The other patient had a normal amount of amylase in the blood. On the other hand, one patient with cholelithiasis and with no serum lipase, had an elevated blood amylase.

Renal Insufficiency.—Patients were placed in the category of renal insufficiency on the basis of blood nonprotein nitrogen levels above 50 mg. per cent. The serum of nine of thirty-one patients contained lipase. It was not possible to determine from the record in which patients the nonprotein nitrogen was rising or falling, although this factor may have influenced the serum lipase value. In those patients in whom serum amylase was determined, normal amounts were found.

Diabetes Mellitus.—The serum in one of ten patients contained lipase. This patient had a severe case of diabetes, out of control at the time. Two additional patients with pancreatic insufficiency showed no elevation of serum lipase.

Other Diseases Without Evidence of Renal Insufficiency.—The serum in three of forty-three patients contained lipase. One of these patients had a carcinoma of the right kidney which had extended beyond the confines of the capsule. There was no evidence that pancreatic structures were involved. The serum amylase was normal and jaundice was absent. Another patient was found at operation to have a peritonitis involving the parametrium and limited to the pelvis. Lipase persisted in the serum of this patient for over two weeks. The third case of biliary cirrhosis with a serum lipase which persisted for fifteen months, has been mentioned. The reason for the presence of lipase in the blood of these three patients is obscure. The cases without serum lipase included gastrointestinal disorders, metabolic disturbances, endocrine abnormalities, cardiovascular disease and inflammatory disease.

TABLE IV. HEPATITIS

NUMBER	SEX	NONPROTEIN NITROGEN (MG. PER CENT)	BILIRUBIN (MG. PER CENT)	THYMOL TURBIDITY	LIPASE (UNITS PER C.C.)	COLOR DENSITY IN KLETT UNITS		DIAGNOSIS
						WITHOUT TAURO-CHOLATE	WITH TAURO-CHOLATE	
M7638	M	39	2.9	65	0	365	330	Infectious hepatitis
M10350	F	27	30.1	20.3	0	315	170	Chronic infectious hepatitis
M10831	F	23	100*	58.7	0	298	250	Infectious hepatitis
M19556	M	50	17.3	9.9	0	356	213	Infectious hepatitis
M19085	M		1.3	21.5	0	459	387	Infectious hepatitis
M19224	M		20.6	84.7	0	349	288	Infectious hepatitis
M10759	F	45	15.9	28.8	0	305	214	Homologous serum jaundice
M10954	M		21*	9.4	0	450	270	Homologous serum jaundice
M16802	F		19.2	26	0	545	410	Homologous serum jaundice
M17947	M	36	22.7	18.2	0	445	178	Homologous serum jaundice
M17654	F	39	47*	58	0	505	199	Homologous serum jaundice
M19693	F		16.5	100	0	466	300	Homologous serum jaundice
M19717	M	22	13.5	6	0	238	214	Homologous serum jaundice
M19543	F		12.3	20.9	0	562	406	Homologous serum jaundice
M18729	F		2.2	21.7	0	516	440	Homologous serum jaundice

*Icteric index.

TABLE V. SUMMARY

CATEGORY	TOTAL NUMBER OF PATIENTS	PATIENTS WITH LIPASE IN THE SERUM	
		NUMBER	PER CENT
Pancreatitis	13	5	38
Carcinoma of pancreas	6	1	16
Common duct obstruction	15	8	53
Hepatitis	15	0	0
Gall bladder disease	21	2	9
Renal insufficiency	31	9	29
Diabetes mellitus	10	1	10
Others	43	3	7

DISCUSSION

Increase in the lipase content of blood has been considered to be a specific test for obstruction of the pancreatic duct.[8] Elevations in serum lipase have been reported in 97 per cent[12] and 81 per cent[13] of cases of pancreatitis, and in almost 100 per cent of experimentally induced pancreatitis in dogs.[3, 7] Lipase as determined by our method was found in the serum in only five of thirteen cases of pancreatitis and in two cases reported earlier.[2] In cases of carcinoma of the pancreas, elevations in serum lipase as determined by other methods were reported in 40.5 per cent[12] and 53.5 per cent[13] of two series. We found lipase in the serum in 29 per cent, i.e. (one of six), cases herewith reported, and one case reported earlier.[2]

Increased serum amylase, but not increased lipase has been reported in common duct obstruction.[14] In our fifteen patients with common duct obstruction, eight showed serum lipase activity. Lagerlöf reported that lipase did not increase in hepatitis with jaundice.[15, 16] This was also true of our fifteen patients with hepatitis. These preliminary results suggest the possible value of the level of serum lipase activity, determined by this method, in the differential diagnosis of obstructive versus hepatocellular jaundice.

Changes in the level of serum amylase due to renal insufficiency were reported in 1915.[17] There are, however, no reports of similar changes in serum lipase. In this series, 29 per cent of thirty-one patients with blood nonprotein nitrogen above 50 mg. per cent showed lipase activity in their blood. Since there is no lipase in the blood of normal subjects[2] and considerable quantities of lipase in the urine,[9] impairment of kidney function could understandably affect the normal low renal threshold for lipase and account for the appearance of lipase in the blood in patients with renal insufficiency. Urinary measurements of lipase were made concomitantly with serum determinations in the last forty-five patients. The variation in urinary lipase in these pathologic states was of the same order as pointed out for normal states,[9] and no correlation could be noted between urinary lipase and serum lipase, or between urinary lipase and the pathological process. Although lipase appeared in the blood in only one of every four cases of nitrogen retention, these observations indicate that the status of renal function must be considered in evaluating the significance of lipase activity in the blood.

The failure of some patients with acute pancreatitis to show serum lipase activity in the face of an elevated serum amylase remains obscure. Similarly, the elevations of serum lipase in the cases of pelvic peritonitis, biliary cirrhosis, and uncontrolled diabetes remain unexplained to date.

The levels of esterase activity in the blood of these patients, indicated by the color density of the tube without sodium taurocholate, did not show striking or consistent correlations with the pathologic state. In one patient with pancreatitis and in another patient with undiagnosed abdominal pain, the esterase activity was particularly high, although a significant quantity of lipase was not present. By other methods for determining lipase, this greater esterase content might have given an elevated value for lipase due

to hydrolysis of the substrate, olive oil. This may in part account for the larger per cent of lipase elevations reported with other methods than our own. The fact that lipase activity may be estimated exclusively, conveniently, and with a high degree of sensitivity in the presence of varying amounts of esterase, warrants further study of clinical material with this colorimetric method.

SUMMARY

By the use of a colorimetric method for measuring serum lipase activity, lipase, which is not found in the serum of normal subjects, was found in the blood of some, but not all, patients with pancreatitis and common duct obstruction. Since none is observed in hepatitis, measurement of serum lipase might be useful in the differential diagnosis of jaundice. Since serum lipase is occasionally elevated in renal insufficiency, the significance of an elevated serum lipase must be interpreted with due regard for the state of renal function.

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THE INDIVIDUAL ESSENTIAL AMINO ACIDS IN PLASMA AND URINE OF SURGICAL PATIENTS

With Particular Reference to a Comparison Between Well-Nourished and Malnourished Patients

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A RELATIONSHIP between fasting plasma level of alpha amino nitrogen and preoperative nutritional status of the surgical patient was reported by Man and co-workers[26] in 1946. They noted that a low fasting plasma level of alpha amino nitrogen (below 4 mg. per cent) was invariably associated with poor nutritional status of the preoperative surgical patient.

As measurement of alpha amino nitrogen is a summation of amino nitrogen from more than twenty individual amino acids, it does not give any indication of the levels of the various individual amino acids.[32] However, certain of the individual amino acids (the so-called essential amino acids) which cannot be manufactured by the body from other nitrogenous substances, are of particular significance in nutrition.[30, 31, 34-37] Accordingly, a knowledge of the plasma levels of these individual essential amino acids would appear to be particularly important in assessing the nutritional status of the preoperative surgical patient.

Despite the great importance of the essential amino acids in protein metabolism, there have been few studies of the levels of these individual amino acids in biologic fluids of human beings until the recent work of Hier and Bergeim.[17-20] The main reason for this has been that the methods available for the determination of individual amino acids in biologic fluids have been tedious and frequently inaccurate. However, during recent years, microbiologic methods for the assay of individual amino acids have been developed. These methods permit the quantitative determination of individual amino acids in biologic fluids with a relatively high degree of accuracy. By the utilization of these methods, a study has been made of the fasting plasma levels of the individual essential amino acids in a group of surgical patients. In addition, the levels of the individual essential amino acids have been determined in the urine of a small group of surgical patients.

REVIEW OF THE LITERATURE

The majority of the studies of the amino acids in blood and urine of patients and animals with pathologic conditions have consisted of the measurement of amino nitrogen. Elevations of the plasma amino nitrogen level have been reported by several authors in conditions characterized by marked liver damage such as acute yellow atrophy of the liver,[33, 41, 44] hepatolenticular degeneration (Wilson's disease),[11] experimental phosphorus[28] or hydrazine poisoning,[25] and experimental yellow fever.[43] An increased urinary excretion of

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amino nitrogen was noted in association with these plasma level changes. Liver damage of moderate to mild degree has not been found to cause variations from the normal plasma amino nitrogen levels.[1, 15]

Elevation of plasma amino nitrogen level also has been reported to occur in conditions such as nephritis or uremia which are characterized by marked renal damage.[2, 22] In most instances, however, any marked elevations are preterminal phenomena. On the other hand, a decline in plasma amino acid concentration has been noted in acute nephrotic crises.[12] Likewise, a decrease in level has been reported in patients with pneumococcus pneumonia, measles, and scarlet fever.[13] A decrease in plasma amino nitrogen level was noted by Man and co-workers,[26, 27] as previously mentioned, in malnourished preoperative surgical patients suffering from various diseases. Frankl, Martin, and Dunn[14] have studied the urinary excretion of tryptophane, histidine, and cystine in fifty-seven patients suffering from varying pathologic conditions. They found that high urinary amino acid excretion was present in some cases of diabetes mellitus, acute infection, pregnancy, and liver disease. Hier[19] found no consistent variation from normal plasma levels of certain of the individual amino acids in patients with cirrhosis, hypertension, or pregnancy. In general, review of the literature indicates that aside from the changes noted in marked liver or kidney damage, plasma amino nitrogen level varies little from disease to disease. It has been suggested by Peters and Van Slyke[32] that the minor variations of plasma amino acid nitrogen which do occur in other pathologic conditions may be marks of malnutrition. As indicated, only a very few studies have been made of the plasma levels of individual amino acids in patients, and accordingly this field is largely unexplored.

METHOD OF STUDY

The individual essential (free) amino acids were quantitatively determined in fasting plasma samples of sixty-three surgical patients having various pathologic conditions. Special selection of the patients was made so as to have two general groups of patients with respect to nutritional status. Thirty-eight of the sixty-three patients were considered to be of poor nutritional status on the basis of one or more of the following factors: loss of 10 per cent or more of the previous normal weight, clinical appearance of emaciation, blood albumin level below the accepted lower limit of normal (4.6 Gm. per 100 c.c. serum).[24] Twenty-five of the sixty-three patients studied were considered to be in good nutritional status with reference to the above criteria. The majority of the patients in the latter group had no history of weight loss and in no case was the weight loss appreciable. The two groups contained patients having approximately the same pathologic conditions although there was necessarily some variation.

The twenty-four hour urinary excretion of the individual essential amino acids was studied in five malnourished surgical patients on ward diets.

For the determination of the individual essential free amino acids of plasma, 50 to 60 c.c. of blood were drawn as a fasting morning sample from each patient

studied. The barrel of the syringe used in drawing the sample was coated with heparin and two drops of heparin were placed in the collecting tube to prevent coagulation of the blood. An additional 5 c.c. sample of blood was drawn and allowed to clot. The latter sample was used for the determination of albumin-globulin ratio. Two cubic centimeters of the well-mixed, heparinized blood were used for the determination of the hematocrit which was done in duplicate using Wintrobe tubes which were centrifuged at high speed for thirty minutes. Two c.c. of the well-mixed, heparinized blood were removed for the determination of the nonprotein nitrogen level of whole blood. The remainder of the heparinized blood sample was centrifuged at 3,000 r.p.m. for one-half hour to separate the plasma from the cells. The filtrate of the plasma was prepared according to the method of Hier.[17-19] Determinations of the levels of the individual essential (free) amino acids were then performed on the plasma filtrate using the microbiologic assay methods of Hier and Bergeim.[17-19] The amino acids determined were: leucine, isoleucine, tryptophane, valine, methionine, threonine, arginine, phenylalanine, histidine and lysine. Arginine and histidine were studied because they are essential in certain lower animals, although they are no longer considered essential for maintenance in man since the work of Rose.[36] Nonprotein nitrogen was determined on whole blood using Hoffman's photelometric modification of the Koch and McMeekin direct Nesslerization Kjeldahl micromethod.[21] Serum albumin and globulin were determined by Hoffman's modification of Howe's method.[21] All analyses were performed in duplicate.

Twenty-four hour urine collections were obtained in five malnourished surgical patients who received the regular ward diet during the period of urine collection. The collections were preserved under toluene at a temperature of 4° C. Both free and total individual essential amino acids were determined according to the methods of Hier and Bergeim.[20] Hydrolysis of samples and dilutions used were, in general, those of Hier and Bergeim. All determinations were performed in duplicate for at least two different dilution levels.

RESULTS AND DISCUSSION

A summary of the data obtained in the study of the individual essential (free) amino acids of plasma of twenty-five patients who had no obvious evidence of malnutrition is presented in Table I. The corresponding data obtained in the study of the individual essential (free) amino acids of plasma of thirty-eight surgical patients who had obvious evidence of varying degrees of malnutrition is presented in Table II.

When the average total values for the ten essential (free) amino acids of human plasma in these two series are compared with the corresponding average total value obtained by Hier[19] in a study of twenty-eight normal individuals (medical students), it can be seen (Fig. 1) that there is little difference between the average total value for normal individuals and well-nourished surgical patients. This small difference is not of statistical significance.[40] On the other hand, the difference between these latter two groups and the average total value obtained in thirty-eight malnourished surgical patients is great, and of very high statistical significance.

TABLE I. QUANTITATIVE STUDY OF THE INDIVIDUAL ESSENTIAL (FREE) AMINO ACIDS OF PLASMA IN TWENTY-FIVE WELL-NOURISHED SURGICAL PATIENTS

	GAMMA/C.C. PLASMA	
	AVERAGE	STANDARD DEVIATION
Leucine	20.6	3.9
Isoleucine	14.3	3.5
Tryptophane	10.0	2.0
Valine	28.4	5.2
Methionine	4.9	2.0
Threonine	18.9	4.4
Arginine	23.7	5.8
Phenylalanine	13.4	3.9
Histidine	12.4	2.2
Lysine	27.3	3.8
Total ten amino acids	174.1	13.6

TABLE II. QUANTITATIVE STUDY OF THE INDIVIDUAL ESSENTIAL (FREE) AMINO ACIDS OF PLASMA IN THIRTY-EIGHT MALNOURISHED SURGICAL PATIENTS

	GAMMA/C.C. PLASMA	
	AVERAGE	STANDARD DEVIATION
Leucine	13.2	3.4
Isoleucine	9.0	2.8
Tryptophane	7.5	2.2
Valine	23.6	5.0
Methionine	2.8	.0
Threonine	15.4	4.7
Arginine	21.5	6.0
Phenylalanine	10.4	3.9
Histidine	9.1	2.2
Lysine	20.1	4.5
Total ten amino acids	131.4	24.6

Fig. 2 compares the average values obtained for each of the individual essential (free) amino acids in the two groups of surgical patients and the normal individuals studied by Hier. With the exception of histidine there is no statistically significant difference between the mean values in the group of well-nourished surgical patients and Hier's group of medical students. However, with the exception of arginine, the mean value for each of the individual amino acids in the group of malnourished patients is appreciably lower than the corresponding values for the other two groups. These differences are statistically very highly significant ("t value ">2.7).[40]

It does not appear that the differences between the two groups of patients are on the basis of plasma dilution, at least as far as can be deduced from a comparison of mean hematocrit levels. The mean hematocrit level for the malnourished group of patients was 41 per cent. The corresponding value for the group of well-nourished surgical patients was 43.5 per cent. Moreover, many of the lowest amino acid values obtained in the group of malnourished patients were in patients with normal or even slightly elevated hematocrit levels.

The finding that the mean levels of nine of the ten individual essential amino acids were significantly less in the plasma of malnourished surgical

patients suggested that these findings might be used as a biochemical index of protein malnutrition. Accordingly, a survey was made of the number of plasma levels of each of the individual essential amino acids in the group of malnourished surgical patients which were lower by more than two standard deviations than the corresponding mean levels in the group of well-nourished surgical patients and in the group of normal individuals studied by Hier. Ninety-five per cent of the normal values should fall within the range of two standard deviations of the mean normal values.[40] Thus, levels below this

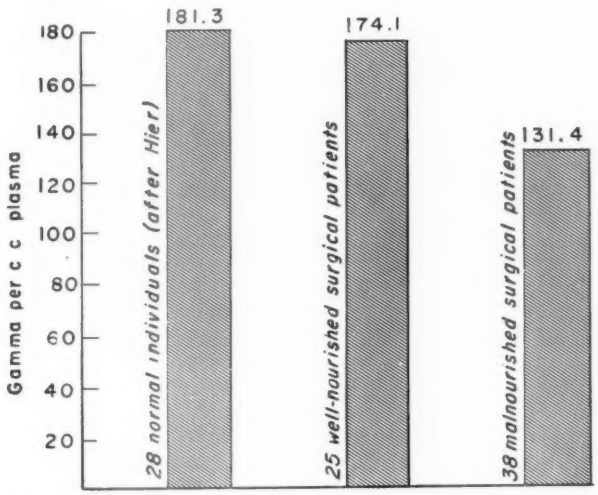

Fig. 1.—Average total values of ten essential (free) amino acids of human plasma.

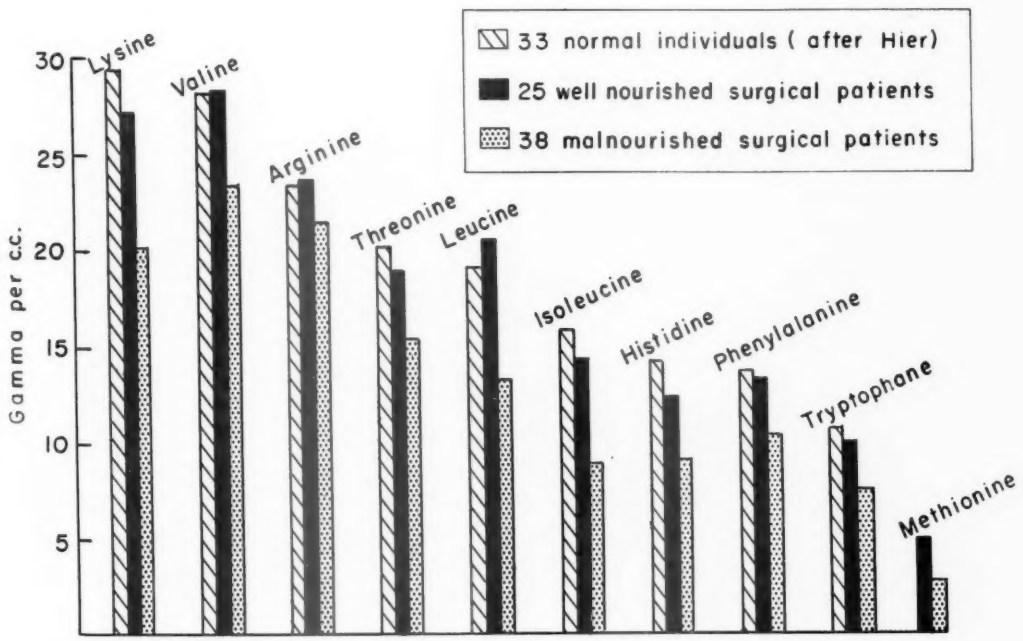

Fig. 2.—Average individual essential (free) amino acids of human plasma.

range would appear to be clearly abnormal and might be used as diagnostic criteria of protein malnutrition. This comparison is presented in Table III. Of the 380 determinations of the plasma levels of the various individual essential amino acids in the group of thirty-eight malnourished surgical patients, 85 plasma levels were found to be more than two standard deviations below the corresponding mean plasma levels in the group of well-nourished surgical patients. One hundred and thirty-three of the 380 plasma levels were found to be more than two standard deviations below the corresponding mean plasma levels in Hier's group of normal individuals.

TABLE III. NUMBER OF DETERMINATIONS OF INDIVIDUAL ESSENTIAL AMINO ACIDS OF PLASMA IN THIRTY-EIGHT MALNOURISHED PATIENTS WHICH ARE LESS THAN NORMAL MEAN VALUES BY MORE THAN TWO STANDARD DEVIATIONS

	COMPARISON WITH WELL-NOURISHED SURGICAL PATIENTS	COMPARISON WITH NORMAL INDIVIDUALS (HIER)
Leucine	19	14
Isoleucine	9	19
Tryptophane	10	11
Valine	5	16
Methionine	0	0
Threonine	6	8
Arginine	3	3
Phenylalanine	2	9
Histidine	14	29
Lysine	17	24
Total ten amino acids	25	20

It seems reasonable to assume that the mean values obtained by Hier in his studies of medical students, presumably free of disease, more nearly represent normal values than the mean values obtained by us in a study of well-nourished surgical patients with diseases or conditions severe enough to require operation. It must also be remembered that the amount of weight loss was one of the criteria utilized by us in the division of patients into well-nourished and malnourished groups. Anyone who has had experience in taking patient histories will attest to the difficulties which exist when attempts are made to elicit information relative to the amount of weight loss. It is therefore conceivable that because of misinformation some patients may have been incorrectly classified as to their nutritional status. It must be further admitted that the criteria utilized by us in making the classification of nutritional status are purely arbitrary and empirical criteria.

The plasma levels of three of the individual essential amino acids were reduced in more than 50 per cent of the malnourished surgical patients by more than two standard deviations from the corresponding mean levels of Hier's group of normal individuals. These amino acids were the following: isoleucine, histidine, and lysine. The total value for the ten individual essential amino acid plasma levels was also reduced in more than fifty per cent of the malnourished patients by more than two standard deviations from the corresponding mean total value of Hier's group of normal individuals. It would thus appear that if a decrease of the plasma levels of the individual

amino acids is to be used as diagnostic evidence of protein malnutrition, then the plasma levels of these three individual amino acids or, perhaps, the total level of the ten essential amino acids would be most important.

The group of thirty-eight malnourished patients was divided into several subgroups for the purpose of evaluation of various factors (Fig. 3). Comparison was made between eighteen patients with carcinoma, and the twenty without carcinoma. Comparison was also made between twenty-one of the thirty-eight patients who clinically appeared emaciated and the remaining seventeen patients who clinically did not appear emaciated despite a history of appreciable weight loss. Also, comparison was made between the thirteen patients with blood albumin levels below the lower limit of the accepted normal levels (4.6 Gm. per 100 c.c. serum)[24] and the remaining twenty-five patients who had normal blood albumin levels (4.6 or more Gm. per 100 c.c. serum). In addition, comparison was made between the eight

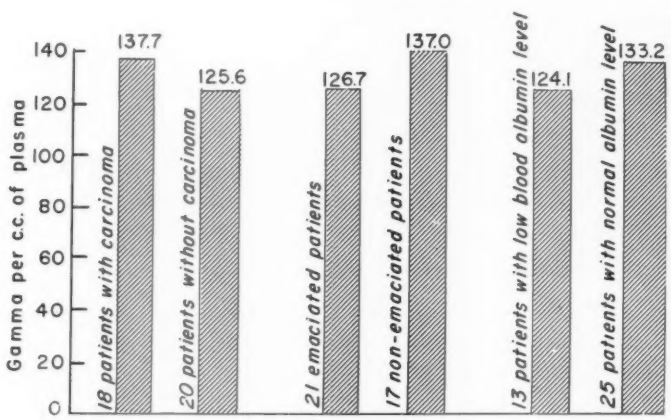

Fig. 3.—Average total values of ten essential (free) amino acids of plasma of malnourished surgical patients.

patients who had evidence of varying degrees of liver damage as judged by one or more liver function tests and the remaining thirty patients who had no evidence of liver damage. In these subgroups there were no statistically significant differences in the average total values for the ten essential amino acids in the plasma of these patients. Also, with a few exceptions there were no statistically significant differences in the levels of the individual essential amino acids on the basis of these comparisons. Leucine and isoleucine are significantly less in the group of patients without carcinoma as compared with the group of patients with carcinoma. Only valine is significantly less in the group of clinically emaciated patients when comparison is made with the non-emaciated patients. Again valine was the only amino acid significantly less in the plasma of patients with low blood albumin level when comparison was made with the remainder of the group patients who had normal blood albumin levels. Isoleucine and valine were significantly less in the plasma of patients with evidence of liver disease when compared with the patients who showed no evidence of liver damage. In all cases, however, all values were significantly

less than those found in well-nourished surgical patients with the exception of arginine, as was previously mentioned. These findings suggest that, in general, the decreased levels of the free amino acids in the plasma of malnourished patients cannot be attributed to any one of the above discussed factors. What is responsible for the minor differences in certain of the subgroups, we are unable to say. In certain instances the series studied is small, and this possibly may be a factor in the production of the differences noted.

The slight difference in the values obtained in patients who had low blood albumin levels as compared with similarly malnourished patients with normal blood albumin levels suggests that a decrease of the free essential amino acids in plasma may be an earlier biochemical sign of protein malnutrition than a decrease of blood albumin levels. As pointed out by Youmans and Patton[45] and numerous other workers, the finding of a low blood albumin level is a late sign in protein malnutrition. Yet, at the present time, it is the only generally used biochemical test for the estimation of protein deficiency. The patients studied in this group were selected because of a history of appreciable weight loss or clinical evidence of malnutrition. Thus, they also, in most instances, represented advanced stages of protein depletion. However, it is interesting that low blood albumin levels were noted in only thirteen of these patients and that decreases in the essential amino acids occurred in the malnourished patients with normal blood albumin levels as well as the patients with low blood albumin levels as well as the patients with low blood albumin concentration. In the thirteen patients with low blood albumin levels, eight of the thirteen total values for the ten individual essential amino acid levels were more than two standard deviations below the corresponding mean total value in Hier's group of normal individuals. Fifty-seven of the 130 determinations of the various individual essential amino acids in these thirteen patients were more than two standard deviations below the corresponding mean levels obtained by Hier in normal individuals.

From our data it is not possible to postulate at what point the decreases in the essential amino acids in plasma occur in the malnourished individual. That the level of the essential amino acids in the plasma may be a relatively sensitive index of inadequate protein nutrition is suggested by the recent work of Kirsner, Sheffner and Palmer,[23] and the work of Henderson, Schurr, and Elvehjem.[16] Kirsner and co-workers found that the free amino acids, with the exception of arginine, were appreciably decreased in a single human subject who was maintained on a diet very deficient in the essential amino acids for a period of six days. Henderson and co-workers found similar changes in the free amino acids of plasma of rats placed on protein-free diets for a week or less. While these studies suggest that the change in the levels of the amino acids in the plasma occurs early in the course of protein deficiency, further investigation in experimental animals is contemplated to establish this point definitely.

On the basis of limited observations in our series it does not appear that the decreased plasma levels of the individual essential amino acids in mal-

nourished patients is influenced by high protein intake immediately preceding the determinations. That is to say, a high protein diet a few days preceding the determinations does not cause the appearance of normal plasma levels of the free amino acids in malnourished patients. To substantiate this statement, the following cases are cited:

PATIENT 37B.—This patient was admitted to the Research and Educational Hospital on Jan. 3, 1950. The patient was placed on a high-protein, high-calorie diet and was observed to eat the diet presented. In addition, the patient was transfused with 3,000 c.c. of whole blood. By Jan. 16, 1950, the patient had gained approximately ten pounds of weight. On Jan. 17, 1950, blood was withdrawn for determination of the individual essential (free) amino acids of the plasma. All of the amino acids studied were markedly reduced below the normal level. The total value for the ten amino acids was only 107.9 gammas per cubic centimeter of plasma.

PATIENT 2B.—This patient was admitted to the Research and Educational Hospital on March 11, 1949. The patient was placed on a high-protein, high-calorie diet and ate the food presented. The patient maintained weight on this program and gained almost two pounds. On March 26, 1949, blood was withdrawn for the determination of the individual essential (free) amino acids of the plasma. All of the individual amino acids studied were below the normal levels. The total value for the ten amino acids was 110.7 gammas per cubic centimeter of plasma.

PATIENTS 19B, 35B, AND 38B.—These three patients were on high-protein diets for periods ranging from one to two weeks before samples were drawn for determination of the individual essential amino acids of plasma. The total values for the ten amino acids of plasma studied in these patients were 119.0 gammas, 127.4 gammas, and 140.6 gammas, respectively, per cubic centimeter of plasma. Likewise the individual amino acids in these patients showed values markedly less than the normal values. This evidence would appear to indicate that the decreased levels of free amino acids of plasma are not restored to normal in malnourished patients by only a few days of high-protein diet.

There is evidence to indicate that some type of dynamic equilibrium exists between the amino acids of the various tissues and plasma.[38, 39] The tissue proteins are constantly being broken down into free amino acids and new tissue proteins are constantly being formed from the free amino acids liberated by the breakdown of protein. It seems probable, therefore, that some type of equilibrium exists between the free amino acids of plasma, the free amino acids of tissues, and tissue protein. This view is supported by the recent work of Thompson, Schurr, Henderson, and Elvehjem,[42] who found that nitrogen deprivation in rats was associated with decreases in the free amino acids of various tissues studied. Further work is contemplated on this problem to establish the exact quantitative relationship between the free amino acids of plasma and tissues, and tissue protein. However, on the basis of the evidence available at the present time, it appears that the decreases in the levels of the individual essential amino acids in plasma are probably correlated with a decrease in the level of the essential free amino acids of tissues, and a decrease of tissue protein.

The magnitude of the mean decrease of each individual essential amino acid in the plasma of malnourished individuals with respect to the accepted normal values is given in Fig. 4. The decreases range from 9.4 gammas for

lysine to 1.9 gammas for arginine per cubic centimeter of plasma. In view of the well-known decrease in blood volume in malnourished patients, it is probable that the magnitude of decrease of each of the amino acids studied is greater than is apparent by simple calculation of concentration per cubic centimeter of plasma.

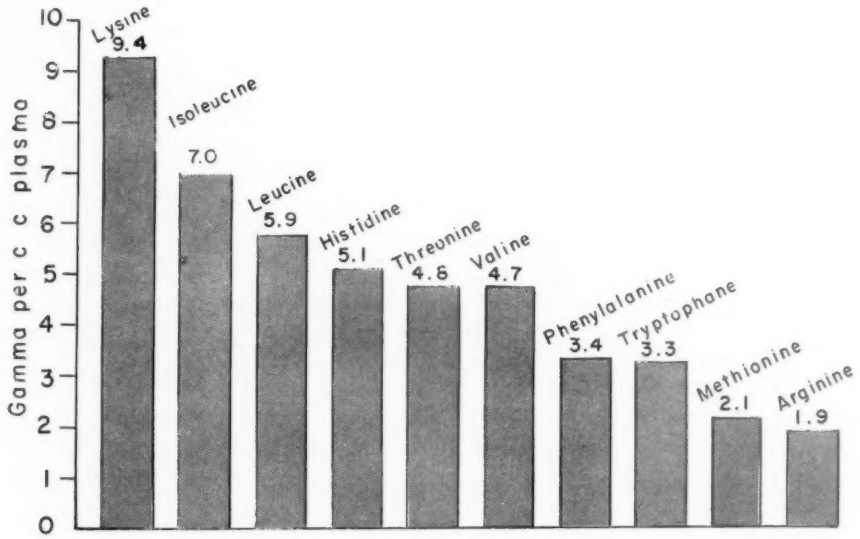

Fig. 4.—Average reduction from normal levels of individual essential (free) amino acids of plasma of thirty-eight malnourished surgical patients.

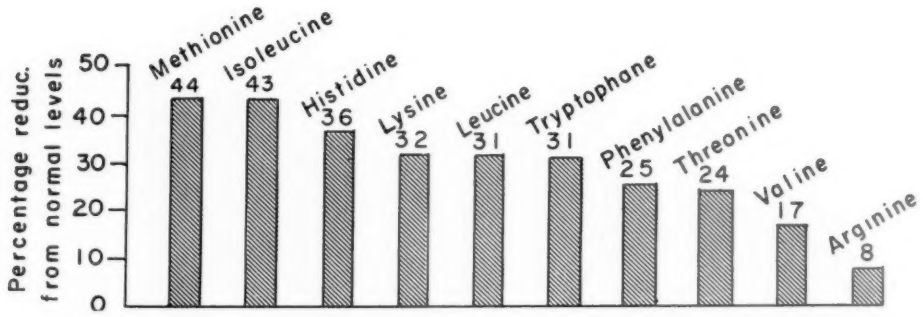

Fig. 5.—Average percentage of reduction of individual essential (free) amino acids of plasma of thirty-eight malnourished surgical patients.

Because the plasma level of the various essential amino acids normally ranges from over 30 gammas to 5 gammas, the decrease in malnourished patients has also been calculated on the basis of percentage reduction of each amino acid. These data are presented in Fig. 5. The percentage reduction varies from 44 per cent for isoleucine and 43 per cent for methionine to 17 per cent for valine and 8 per cent for arginine. This suggests that reinforcement of the diet with added amounts of those amino acids most reduced in malnourished surgical patients might accelerate protein synthesis in such individuals. Investigation of this problem in experimental animals is contem-

plated. It is interesting to note that Croft and Peters[4] found that the loss of urinary nitrogen in burned rats was substantially reduced by the incorporation of added amounts of methionine in the diet. This finding would seem to support the view of Cuthbertson[5-10] that the increased urinary catabolism of protein after trauma was in response to a demand by the body for certain key amino acids for repair purposes. This view of Cuthbertson's might be generalized to consider any disease of long standing or severity to be a form of trauma. This might therefore be a possible explanation for the differing percentage reductions of the varying amino acids. It must be admitted that the work of Croft and Peters has not been confirmed by Meyer, Hirshfeld, and Abbott[29] or Chanutin and Ludewig.[3] However, the theory of Cuthbertson remains an interesting subject for speculation.

The data obtained in the determination of free and total individual essential amino acids in the twenty-four urine collections of five malnourished surgical patients on ward diets indicated that no definite variations were noted in the excretion pattern of the amino acids studied when comparison was made with the published values for normal individuals on average diets.[11, 20] Because of dissatisfaction with the accuracy of reproducibility of determinations of the free amino acids in urine samples the study was not continued.

SUMMARY AND CONCLUSIONS

A study has been made of the individual essential (free) amino acids in fasting plasma samples of surgical patients.

A group of malnourished surgical patients had significantly lower plasma levels for each of the individual essential amino acids, with the exception of arginine, when comparison was made with a group of well-nourished surgical patients and the published normal values of Hier.

Comparison of the individual essential (free) amino acids in fasting plasma samples of well-nourished surgical patients revealed no statistically significant differences when compared with the normal values, with the exception of histidine, which was lower in the well-nourished group of surgical patients.

Decreased levels of the individual essential amino acids of plasma may be an earlier biochemical index of malnutrition than is measurement of blood albumin level.

In malnourished patients there was considerable difference in the amount and percentage of decrease of the various individual amino acids studied. This suggests the need for investigation of the possibility of accelerating protein synthesis in malnourished surgical patients by reinforcing the diet with those amino acids which showed the greatest decrease, especially methionine and isoleucine.

A study of the urinary excretion of the individual essential amino acids in five malnourished surgical patients on an average ward diet revealed no values varying significantly from the published normal values.

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CANNULA FOR EMPTYING THE SMALL BOWEL IN CASES OF INTESTINAL OBSTRUCTION

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WHEN, at operation, a common cannula or empyema trochar is used for aspiration of fluid from the peritoneal cavity, one notices frequently that the wall of the intestine or the omentum is sucked into the holes of the cannula, terminating effective suction.† Moreover, congestion and injury of the bowel with serious potential consequences may ensue.

These disadvantages are more serious when aspiration of the intestinal lumen is tried in cases of obstruction, and this is commonly done by means of the syphon method using a cannula connected to a long tube (Monks,[1] Moynihan[2]). In 1936, I described cannulae for surgical aspiration based on a very simple principle of physics, clearly delineated in Figs. 1 and 2, which show the cannula for drainage of fluids in the abdominal cavity. In this, aspiration is done by the central tube (*1*) which is inside the collecting tube, (*2*) where, by gravity, the fluids are collected passing through the inferior orifices, (*3*) due to the presence of another orifice, (*4*) in the upper portion of the collecting tube, the pressure inside this tube remains constantly equal to that outside it, even when aspiration reaches very high degrees. In view of the fact that the cannula must be maintained in a vertical position during aspiration, it is attached to a handle at a 90 degree angle.

At the same time, based on the same principle, I also constructed a cannula for emptying the intestinal content, from which was later derived the cannula that represents the subject of this article. This one has a lesser diameter and has an external sheath, shaped like the mouthpiece of a flute, which moves axially along the collecting tube. The superior orifice of the collecting tube is substituted for a short tube where a rubber tube is attached, in order to avoid spillage of fluid into the operative field. Use of the instrument is very simple: A purse string suture is placed in the wall of the selected intestinal loop; the instrument is introduced in the lumen of the organ by means of the tip of the external sheath (Fig. 3, *A*). Once the intestinal wall is perforated, the suture is tied against the sheath and the collecting tube assumes the position as shown in Fig. 3, *B*, so the tip of the sheath is replaced by the smooth end of the collecting tube in order to avoid injury to the intestine.

After World War II, I read an article by Burnett, Rosemond, and Caswell,[4] in which they described a device, improvised by Babcock, for drainage of the peritoneal cavity, which is based on the same principle I described. It is referred to by these American authors as a "sump drain." The reading of that

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†The use of the Kenyon-Pool sucker (Ann. Surg. 58: 537, 1913) eliminates this hazard. (Editor's note.)

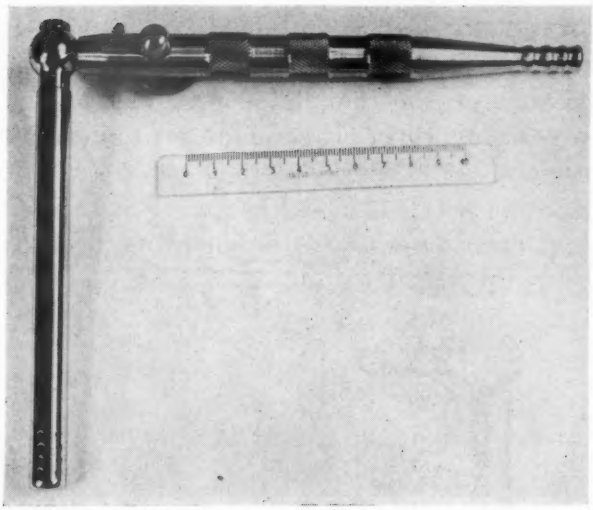


Fig. 1.—Cannula for aspiration of fluids from the peritoneal cavity.

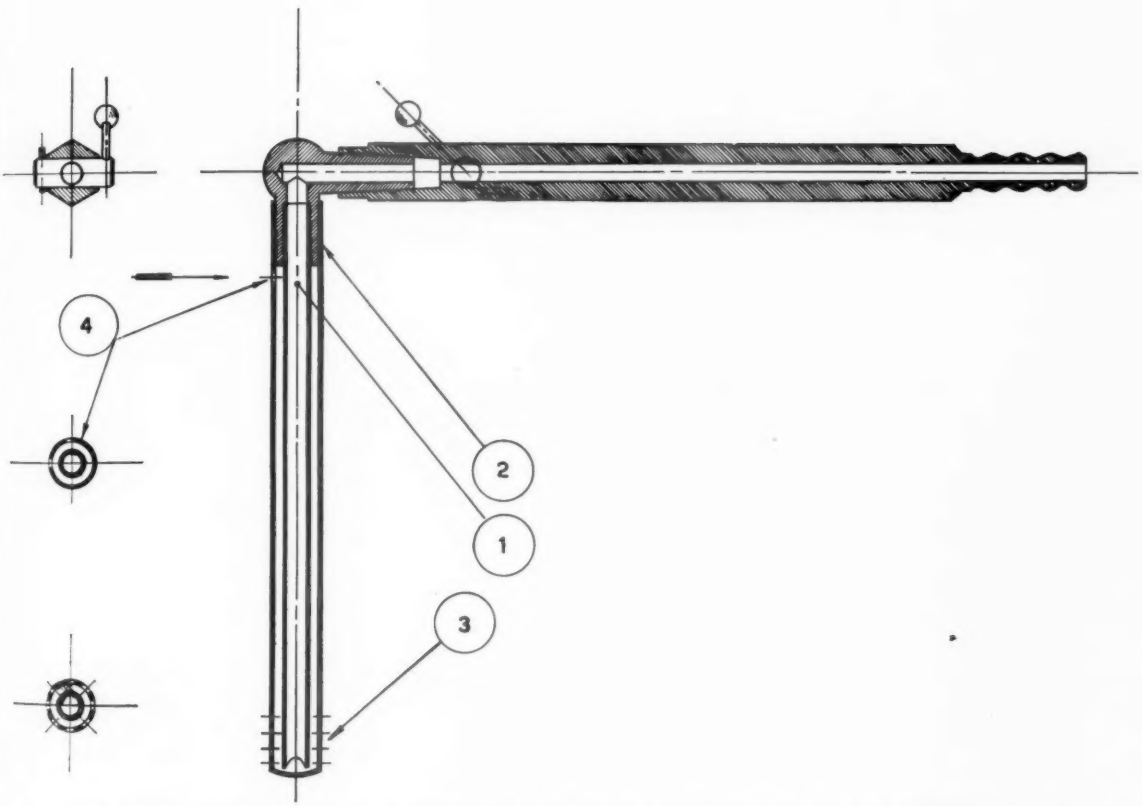
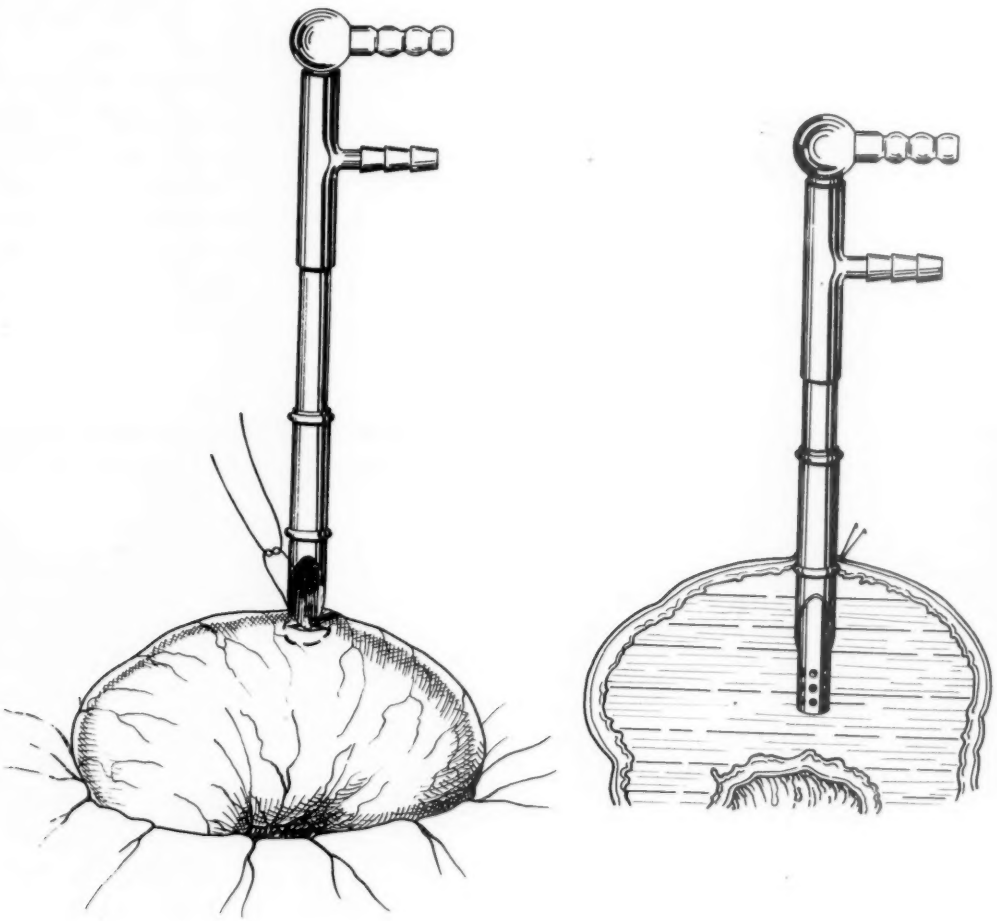


Fig. 2.—Diagram of the same cannula. *1*, Central tube for aspiration; *2*, collecting tube; *3*, lower orifices of the collecting tube; *4*, orifice for air.

article and the magnificent monograph by Wangensteen on *Intestinal Obstructions,*[5] wherein the author describes a device to drain the distended bowel, induced me to develop an improved cannula for drainage of the distended small bowel. From this attempt, the cannula shown in Figs. 4, 5, and 6 was developed after two years of work. It seems to me to constitute a satisfactory solution of the problem.

It is better than the previous model because it is smaller in diameter and because it definitely avoids soiling of the operative field. The technique of its use is clearly shown in Fig. 7.



A. *B.*

Fig. 3.—The former model of cannula for drainage of the small bowel. In (*A*) the cannula is introduced into the intestinal lumen. In (*B*) the collecting tube slides inside the external sheath.

Recently, in view of the scant drainage obtained by the Witzel type of enterostomy which is often performed in late cases of intestinal obstruction, I reflected upon the possibility of leaving in place one of my cannulae which could replace rubber urethral catheters which are generally used for this purpose. To achieve that end I use the cannula shown in Figs. 8 and 9. In two

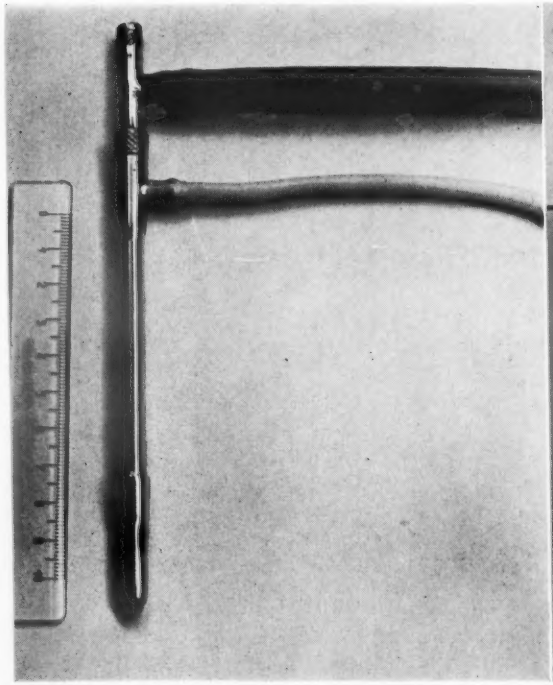


Fig. 4.

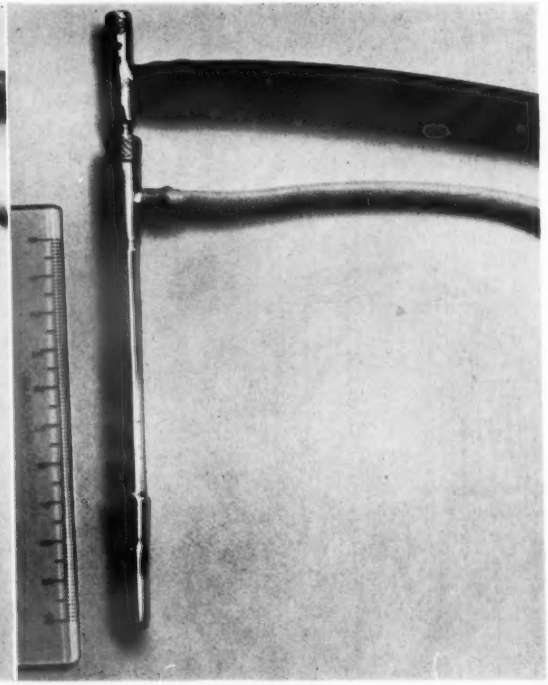


Fig. 5.

Fig. 4.—The new model of cannula for drainage of the small bowel. The pointed tip is outside the collecting tube. The large rubber tube is for aspiration; the small one is for the admission of air.

Fig. 5.—The new model of cannula for aspiration of the small bowel. The pointed tip is pulled inside the collecting tube.

Fig. 6.—Diagram of the new model of cannula for aspiration of the small bowel.

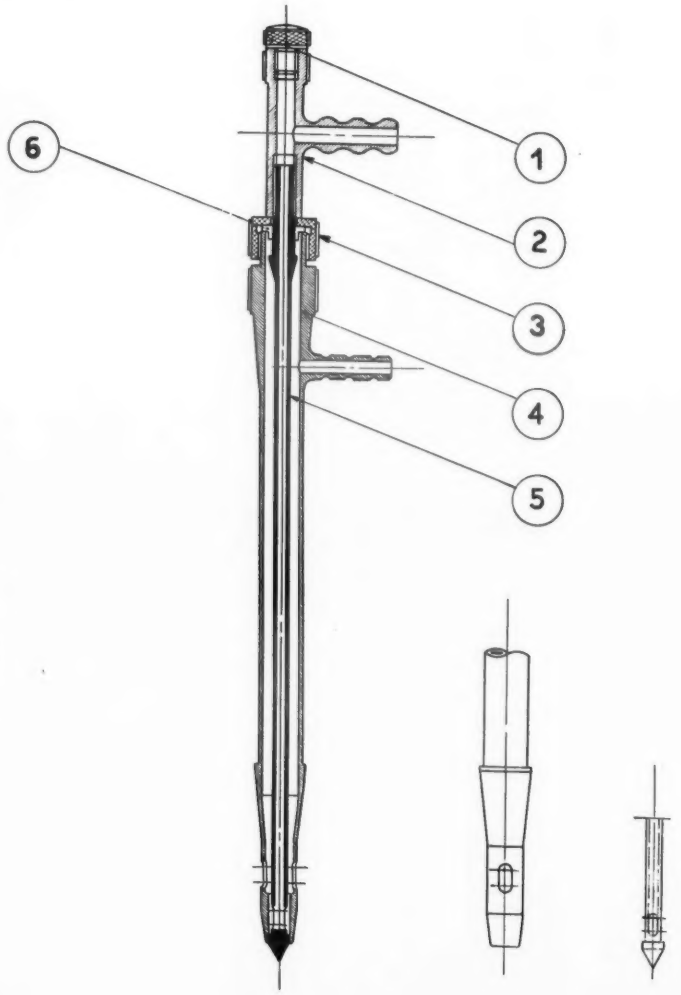


Fig. 6.

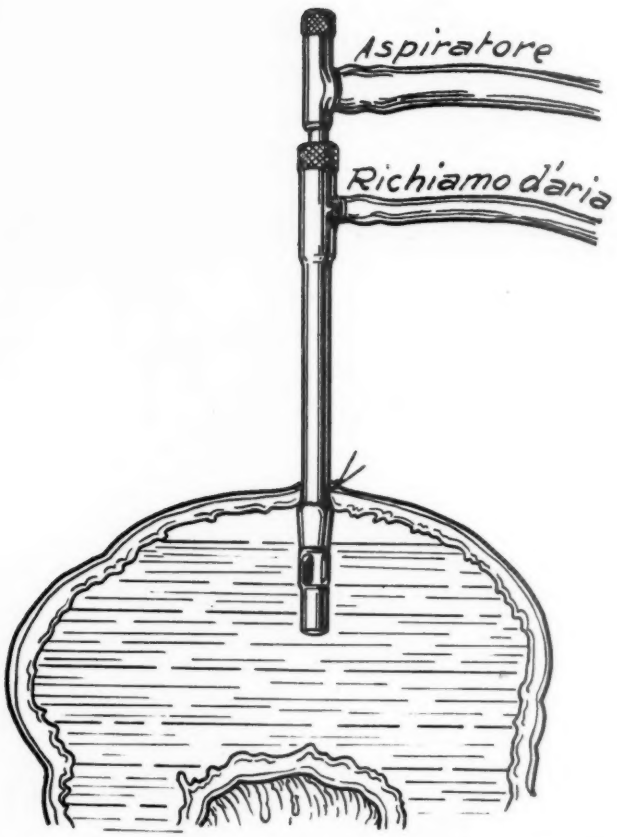


Fig. 7.—The pointed tip of the cannula is pulled into the collecting tube. The aspiration starts.

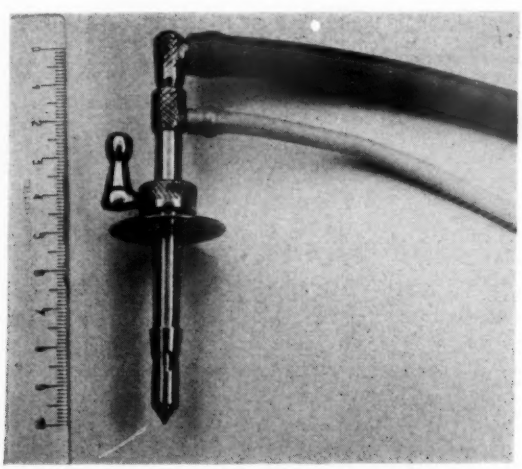


Fig. 8.—This model of cannula may be left in the bowel for continuous postoperative aspiration.

cases in which this cannula was employed for this purpose, the results were excellent. However, it is the use of this cannula in achieving decompression of the distended bowel that I want to emphasize primarily here.

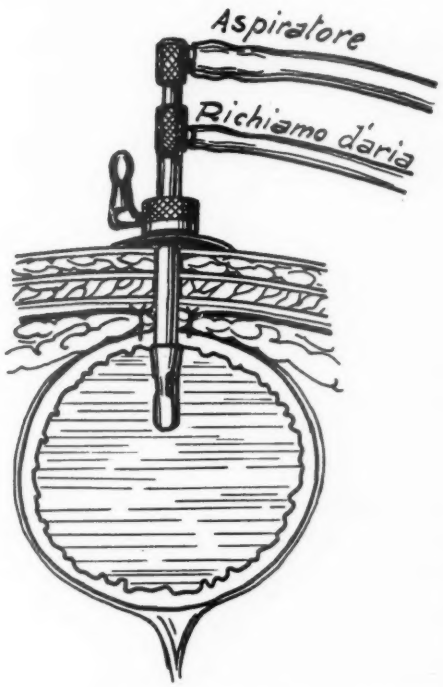


Fig. 9.—The cannula for continuous postoperative aspiration working.

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THE SIGNIFICANCE OF PERINEAL PAIN FOLLOWING RESECTION FOR CARCINOMA OF THE RECTUM

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THE numerous reports on the results of treatment of carcinoma of the rectum contain little information concerning the occurrence of pain in the perineum following abdominoperineal resection. The following study was undertaken in an effort to gain a better understanding of the significance of this symptom. This report is based on clinical and pathologic material from Wadsworth General Hospital, Veterans Administration Center, Los Angeles, Calif., from January, 1947, to January, 1951.

CLINICAL MATERIAL

During the four-year period covered by this report, sixty-six patients were subjected to combined abdominoperineal resection for carcinoma of the rectum (Table I). The operation was considered palliative in eighteen cases because of extension of the tumor to the periaortic nodes, liver, etc. Fourteen of the sixty-six patients developed local recurrence, and the analysis of this group forms the basis of this report.

Because of the relatively small number of cases in this series, detailed analyses of the relation to survival of the location of the lesion and the presence or absence of lymphatic involvement was not made. Excellent reviews by Gilchrist and David,[3] Waugh and Kirklin,[7] and others are available for this purpose. It is of interest that 75 per cent of the lesions in this series arose in the distal 10 cm. of the rectum. This may account in part for the rather high incidence of local recurrence (21 per cent).

Of the fourteen patients who were demonstrated to have local recurrence, recurrence was established from six to thirty months after abdominoperineal resection (Table II). Ten patients developed symptoms of recurrence within eighteen months of operation.

Thirteen of the patients with local recurrence presented themselves with pain in the perineum and the remaining patient later developed this symptom. Other symptoms consisted of sacroiliac or sacrococcygeal pain, loss of sexual potency, and bladder symptoms (dysuria, retention, frequency) (Table III). The pain in the perineum in most instances was quite disabling and the difficulty in management of some of these cases was one of the factors leading to this investigation. In all of the cases, recurrence was demonstrated by surgical biopsy or at autopsy.

Reviewed by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions of the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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TABLE I. SUMMARY OF CASES OF ABDOMINOPERINEAL RESECTION FOR CARCINOMA OF RECTUM

"Curative" operations	48
Palliative resections	18
Total Number of Abdominoperineal Resections	66

TABLE II. INTERVAL BETWEEN OPERATION AND ONSET OF PERINEAL PAIN

6 to 12 months	6
12 to 18 months	4
18 to 24 months	3
Over 24 months	1

TABLE III. SYMPTOMS IN PATIENTS WITH LOCAL RECURRENCE OF CARCINOMA OF RECTUM AFTER ABDOMINOPERINEAL RESECTION

Perineal pain	14
Sacroiliac pain	9
Sacrococcygeal pain	4
Loss of sexual potency	2
Bladder symptoms	10

PATHOLOGY

Microscopic sections from the tumor removed by abdominoperineal resection were studied in the cases of the fourteen patients complaining of perineal pain. Evidence of perineural invasion was found in all but one instance. The perineural lymphatics, particularly in the myenteric plexuses, were often found to be filled with tumor emboli. In several instances direct invasion of the nerve sheath was seen and direct extension along the nerve fibrils was found.

Lymphatic and venous invasion by tumor was frequently noted in conjunction with perineural invasion but there appeared to be no significant correlation in these findings. Since the group studied was small, and because many others have made detailed studies of venous and lymphatic spread, this aspect is not covered in detail in this report; however, it appeared significant that six of the fourteen cases in this series were not found to have regional lymphatic extension (Table IV).

TABLE IV. OCCURRENCE OF LYMPH NODE METASTASIS IN FOURTEEN CASES WITH LOCAL RECURRENCE

Number with lymph node metastasis	8
Number without lymph node metastasis	6

TREATMENT

The variety of methods and medications in the records of the patients in this series indicates the difficulty encountered in controlling the pain. All patients required narcotics in some form. The majority required increasing doses of morphine or Demerol.

Direct attack upon the palpable recurrent lesion in the perineum was employed in three patients with uniformly poor results. Presacral neurectomy

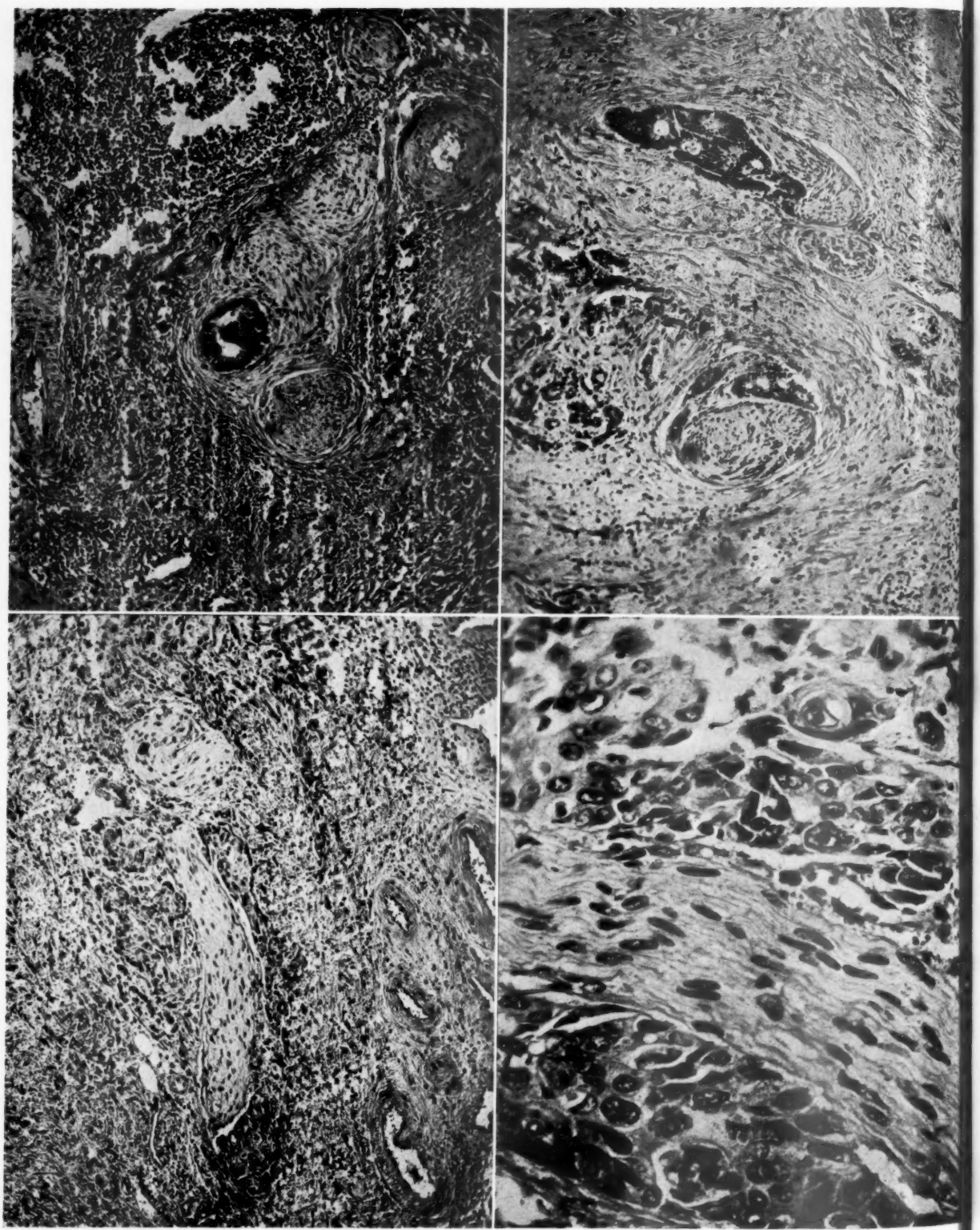

Fig. 1.—Photomicrographs demonstrating perineural invasion in three cases in the series of patients with perineal pain (the lower right photograph is ×450, the others ×160).

was combined with local excision in one of these patients without relief of symptoms.

Regional nerve blocks with alcohol and local anesthetics were of temporary benefit in two cases. Relief of pain for six to twenty-four hours was experienced. Local infiltration of the perineum was not successful.

Palliation was obtained with x-ray therapy for varying lengths of time in six patients. Two patients had three courses of x-ray therapy with decreasing relief of symptoms with each series of treatments.

Cordotomy was employed in one patient with satisfactory relief of pain. Most of the patients were presented to the neurosurgeons too late in the course of their disease to warrant consideration of cordotomy or similar surgical procedures for relief of pain. This was usually due to reluctance on the part of the patient or his family to accept such intervention. Occasionally it appeared to result from the lack of histological demonstration of recurrence. In such cases, the failure of various other methods resulted in delay in referral for neurosurgical assistance.

DISCUSSION

Recent reports of large series of carcinoma of the rectum have emphasized the prognostic importance of the location of the lesion, the presence or absence of regional lymphatic metastases, and venous invasion by the malignant lesion.

The significance of the relation of the lesions to the pelvic peritoneal reflection has been stressed by Gilchrist and David,[3] Sunderland,[6] and Waugh and Kirklin.[7] These reports have demonstrated that carcinoma of the rectum originating below the level of the peritoneal reflection carries a much poorer prognosis than does that originating above the level of the peritoneal reflection. Bacon and Sauer[1] further indicated that lesions in the lower rectal segment have several routes of spread in contrast to the more proximal lesions where the superior hemorrhoidal vessels and accompanying lymphatics offer the principal route of metastasis. It is worthy of note that thirteen of the fourteen patients in the group reported here had carcinoma originating below the peritoneal reflection.

Lahey[4] has stressed the low survival rate when blood vessel invasion can be demonstrated histologically. This applies principally to the resulting distant metastases rather than to local recurrence. Sunderland[6] found that venous invasion was related to the depth of penetration of the bowel wall, lymphatic invasion, and anaplasia, and occurred most frequently in the lower rectal segment.

Recently Dunning, Jones, and Hazard[2] studied the factors influencing survival after operation for carcinoma of the rectum, and concluded perineural extension, as well as venous invasion, was of grave prognostic significance. Eight of the ten patients in their series, in whom perineural involvement was demonstrated, succumbed to carcinoma within three and one-half years of operation. The demonstration of perineural extension in thirteen of the fourteen patients with local recurrence in the present series supports the impor-

tance of their findings. It is of further significance in regard to the etiology of perineal pain. Two of our patients had invasion of the sacrum at one of the foramina.

Indirect support of the importance of perineural invasion in the role of local recurrence of carcinoma of the rectum is given by Pfeiffer and Miller.[5] They concluded from their study of 114 cases of abdominoperineal resection for carcinoma of the rectum below the peritoneal reflection that the local recurrence rate was not influenced by the presence or absence of involved nodes in the tissue removed at operation.

From these findings it would appear that further investigation should be directed to more conclusive determination of what influence perineural invasion has upon local recurrence of carcinoma of the rectum after abdominoperineal resection.

The correlation of pain in the perineum with local recurrence and with perineural extension in this series is striking. Perineal pain in this group was associated with local recurrence of carcinoma in each case. The difficulty in management of these cases and the frequent heavy dosage of narcotics required suggest that earlier consideration of neurosurgical intervention is indicated.

SUMMARY AND CONCLUSIONS

Fourteen patients with perineal pain following abdominoperineal resection of the rectum for carcinoma were studied. The findings suggest a direct correlation between local recurrence due to perineural invasion by carcinoma and the occurrence of the perineal pain. The patients in whom this pain developed all were found to have recurrent carcinoma. Local recurrence would appear to be influenced by perineural invasion of the primary lesion, much as distant spread is correlated with lymphatic and venous invasion. Persistent pain in the perineal region following abdominoperineal resection is almost conclusive evidence of local recurrence of carcinoma.

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THE REPAIR OF CRANIAL DEFECTS WITH ILIAC BONE

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REED O. DINGMAN, M.D.,** ANN ARBOR, MICH.

THE use of fresh autogenous iliac bone for the repair of cranial defects is a very worth-while and reliable method of cranioplasty. During the past two and one-half years at the University Hospital we have utilized this procedure with increasing frequency and satisfaction. We now have fourteen cases in our series. Figures in the text are representative.

We feel that iliac cranioplasty is indicated for: (1) The repair of cranial defects too large for an osteoperiosteal type of graft from another portion of the skull (Figs. 1 and 2); (2) For reconstruction of defects where careful contouring is essential for the reconstruction of margins, ridges, or prominences of the skull (Figs. 3 and 4).

There is no doubt that the employment of autogenous bone, where applicable, is to be preferred to the use of foreign materials such as Vitallium, tantalum, and the resins, for the following reasons:

1. The use of autogenous grafts is physiologically sound, allowing for a normal method of bone healing.

2. Iliac bone is easily available and because of its accessibility may be removed in large amounts from one or both ilia. The great abundance of bone makes it possible to repair skull defects of almost any size (Fig. 5). The quality of rigidity with workability makes iliac bone highly desirable for cranioplasty.

3. Contouring is easily achieved so that a more faithful reproduction is obtained (Fig. 6). It has been our experience that reconstruction of the supraorbital ridge with tantalum or other materials is unsatisfactory in most cases. A well-fitting plate is quite difficult to shape in the low frontotemporal region. Iliac bone is more easily fashioned.

4. Slipping or springing, seen occasionally with metal plates, does not occur with a bone graft.

5. Should air or angiographic studies ever be required following iliac cranioplasty, radiographic visualization through the graft is possible (Fig. 7).

It is our impression that the danger of infection or foreign body reaction is not nearly as great with use of fresh autogenous iliac bone as with one of the inert nonbiologic materials. We have had no postoperative infections in any of our bone graft cases.

Bone grafts in the skull are more resistant to trauma than are metallic or acrylic plates. Foreign body reaction or infection following relatively minor injury is the chief cause of failures in cranioplasty with tantalum, Vitallium, and other foreign materials. This is unlikely when bone is used.

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Fig. 1, *A*.

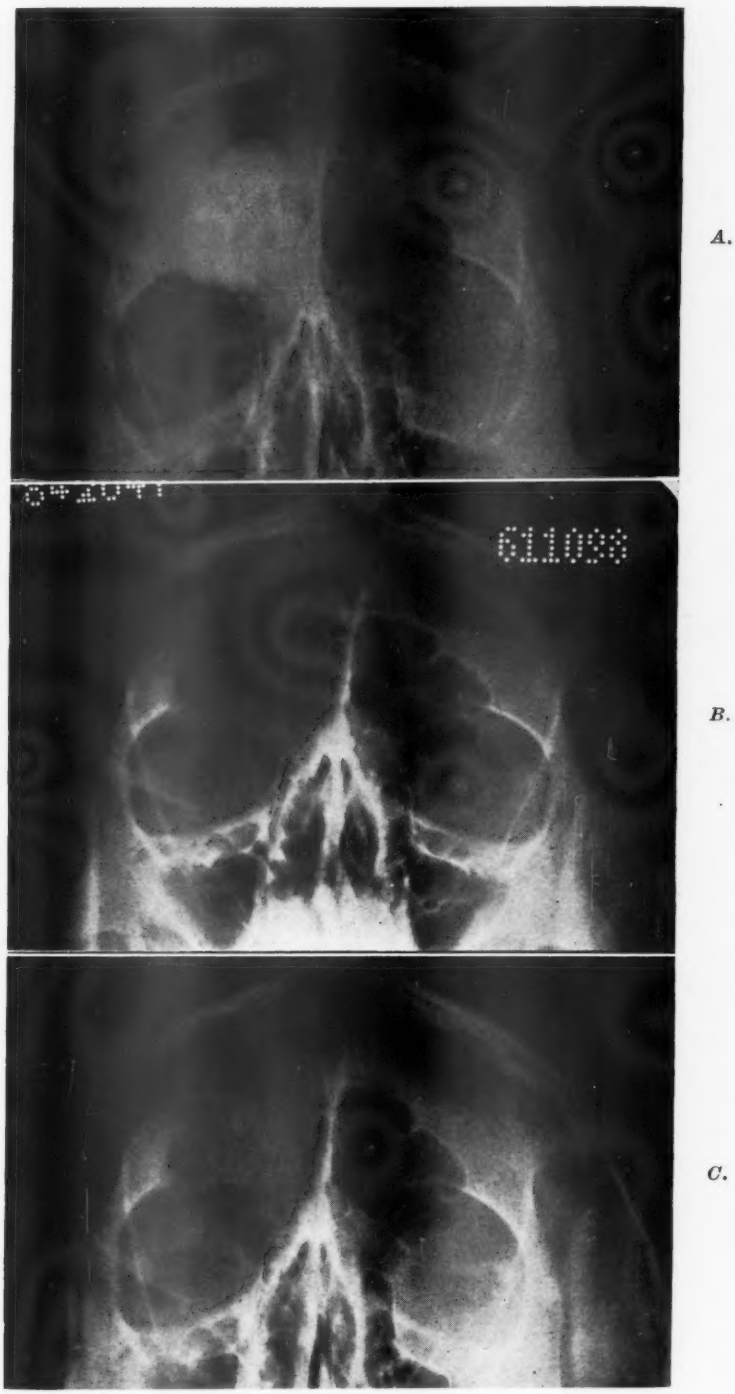
Fig. 1, *B*.

Fig. 2, *A*.

Fig. 2, *B*.

Fig. 1.—*A*, Sagittal view of postoperative defect that has been grafted. Patient had a sarcoma invading the frontal bone and it was removed. A tantalum cranioplasty followed, but infection developed, requiring removal of the plate. *B*, Lateral view of the graft, two weeks postcranioplasty.

Fig. 2.—*A*, Sagittal view of grafted posttraumatic defect, four months postcranioplasty. *B*, Lateral view of same defect. Note small bone islands which were present over the dura prior to grafting.



A.

B.

C.

Fig. 3.—*A*, The area of increased density involving the right frontal bone and sinus is a sclerosing osteoma. *B*, Defect produced following removal of tumor. *C*, Iliac graft faintly visible in defect.

With injury to the scalp directly over the plate, there is great danger of necrosis and subgaleal infection necessitating removal of the plate. We feel that such a complication over a healed bone graft is quite unlikely, since space for potential infection does not exist and the blood supply to the scalp is likely to be more adequate.

6. Another advantage of less importance than the others is that the occasional complaints of discomfort in response to extremes of heat and cold sometimes resulting from large metallic plates are eliminated with the use of bone. Bone is a nonconductor of thermal changes.

A. *B.*

Fig. 4.—*A*, Defect following removal of osteoma. Same patient as seen in Fig. 3. *B*, Postiliac cranioplasty.

There is one disadvantage in this method as compared to tantalum cranioplasty. The operation is of greater magnitude in that two procedures, though carried on simultaneously, are required. This disadvantage is minimal in the light of the excellent end results. An additional operating team is necessary in order to keep the operation time to a minimum. Occasionally during neurosurgical procedures a cranial defect is created that had not been anticipated. Some of these are best repaired immediately. In such instances it is easier to fashion a metallic plate at the table rather than delay, awaiting preparations necessary to obtain an iliac graft.

The technique of obtaining the graft, as well as contouring it, is relatively simple. The patient is placed on his back with the hip selected as the donor side elevated and slightly rotated. By using two operating teams the graft can

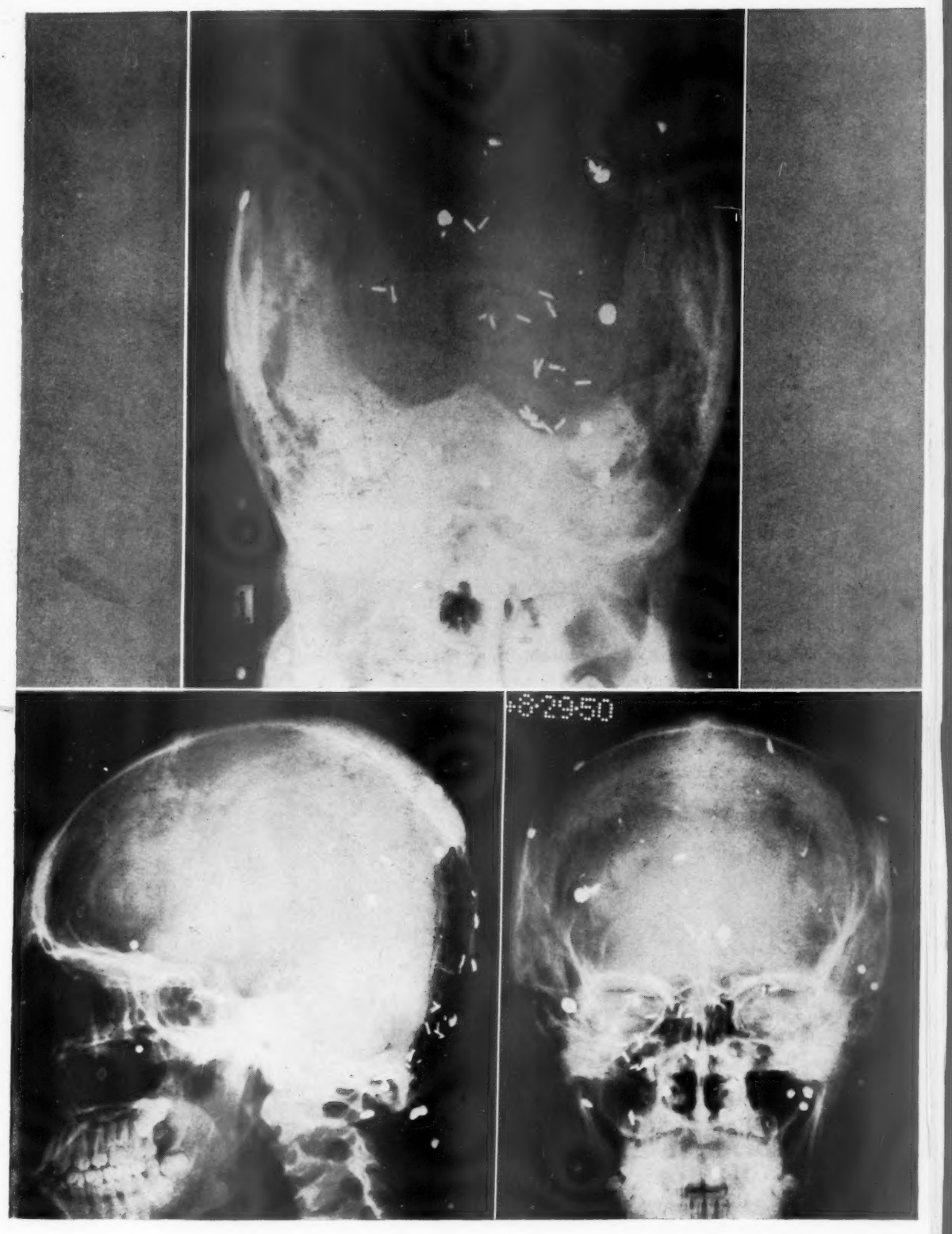
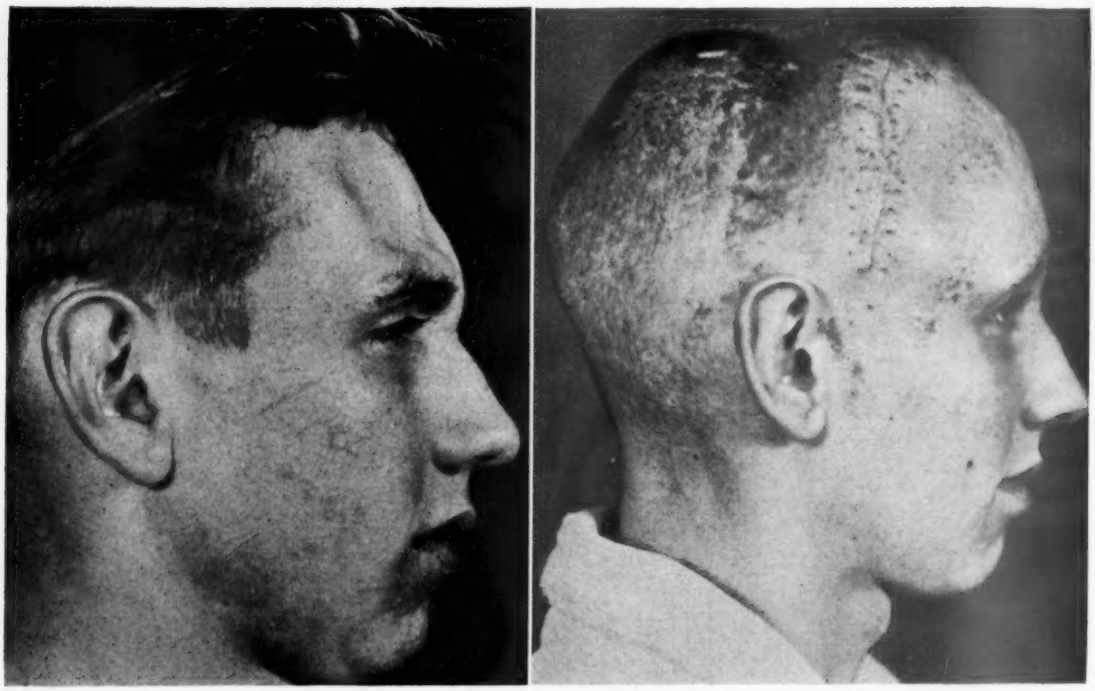


Fig. 5.—*A*, Postoperative occipital and suboccipital defect resulting from osteomyelitis secondary to a shotgun injury. Note multiple pieces of buckshot both intra- and extracranial. *B*, Lateral view showing graft in place, ten months postcranioplasty. *C*, Saggital view; wire sutures for holding graft can be seen.



A. *B.*

Fig. 6.—*A*, Precranioplasty profile. *B*, Following cranioplasty.

A. *B.*

Fig. 7.—*A*, Lateral view two weeks following iliac cranioplasty to a postoperative defect. *B*, Clear visualization of a pneumoencephalogram through the graft three months after cranioplasty.

be obtained by the time the area of the defect has been prepared. To reduce the possibilities of cross contamination two separate instrument tables are set up, one for obtaining and shaping the graft and the other for preparing the recipient site and fixing the graft within it. A curvalinear incision, approximately five inches in length, beginning at the anterior superior spine, is made over the crest of the ilium. The fascial attachments of the abdominal, iliacus, and gluteal muscles are separated at the crest and then stripped subperiosteally from both the inner and outer surfaces of the ilium. The exact donor site depends largely on the contour required to correct the defect. Because of the unusual configuration of the ilium there is considerable difference in the shape of the crest and the bone beneath it in the posterior as compared to the anterior portion. This provides a source of bone of varying conformation so that one area of the ilium is often more suited than another to the particular contour of the graft desired. It is helpful prior to operation to visualize the approximate size and shape of the graft that will be needed. A preoperative estimate of the amount of bone can easily be made and the final contouring of the bone facilitated by the use of a sterile pattern that can readily be prepared before the operation is undertaken. A sterilizable "cast stone" model and pattern of the defect are made from a plaster mold of the patient's defect. A study of the pattern in contact with a dry ilium will enable the operator to predetermine the donor site that will provide the optimum in the way of contour, and quality of bone. This model may be used at the worktable to facilitate contouring of the graft. In no instance should the bone be removed further anteriorly than within 2 cm. of the anterior iliac spine. Preservation of the spine prevents an unsightly deformity of the hip. The approximate outline of the graft to be taken is marked on the exposed ilium and the segment removed with sharp chisels. Damage to the surrounding soft tissues is prevented by retraction over abdominal packs. Either a full-thickness graft can be obtained (Fig. 8, *A*) or, if desired, the crest may be preserved. In such cases the bone of the crest is split leaving the outer cortex in place. The iliac bone thins considerably below the crest so that the remainder of the graft must be full thickness (Fig. 8, *B*). For repair of very large defects a full-thickness section of ilium may be split after removal and the pieces wired together to provide greater coverage. Bleeding from the cancellous portion of the donor site may be brisk but is controlled entirely with Gelfoam (used similarly to bone wax) and hot packs. The fascia of the stripped muscles is then approximated with interrupted 32 gauge stainless steel wire sutures and the remainder of the wound is closed in layers. A small Penrose drain is inserted to prevent clot accumulation in the donor area. It is removed in two days.

In the meantime the cranial defect is being prepared to receive the graft. If possible, the scalp incision should be made 2 or 3 cm. distal to the perimeter of the defect and not traversing it. The bone edges are freshened and excessive scar tissue over the exposed dura is removed. A reproduction of the shaped graft desired is obtained by a mold of quick-setting sterile dental

compound. This material becomes quite pliable when placed in warm water and can be quickly formed. It hardens quickly when cool, sterile water is poured over it. This model shows the exact size and shape of bone necessary to bridge the defect and is of considerable aid in the shaping of the graft. Most of both the inner and outer cortex of the graft can be removed if required. The edges of the graft can be shaped largely with a rongeur. The surface contour changes can best be made with a sharp chisel or osteotome. A dental drill, using a rotary saw and large burr, are helpful instruments but not necessary. A heavy file can be used to smooth sharp edges. As the graft is thinned down additional shaping can be done by bending the margins with large flat pliers. The graft is then wired into place and any small remaining defects around the periphery are filled in with bone chips.

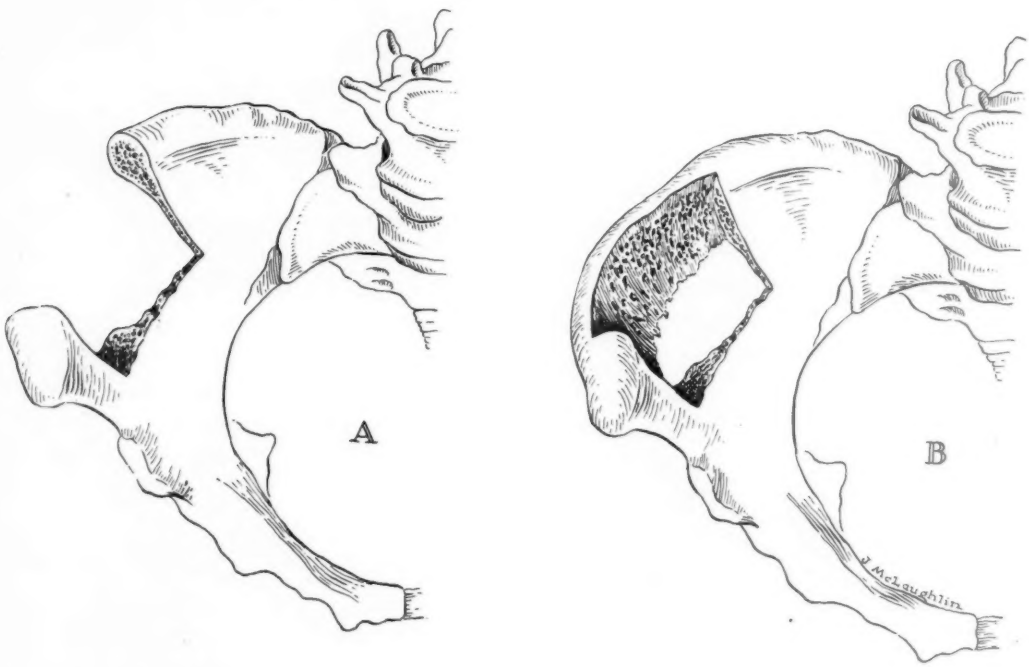


Fig. 8.—*A*, Donor site with crest included in graft. *B*, Donor site with the crest preserved.

Postoperatively the patient is kept in bed four days and then ambulation is encouraged. There are usually complaints of pain in the donor site. This pain can be largely controlled with narcotics. Within a week or ten days the patient has no disability resulting from bone removal.

The grafts become solid within a few weeks. Almost all of them are seen by x-ray to be less dense than the surrounding skull because of the difference in cortical thickness. After three or four months they may show a slight additional decrease in density which is an indication of viability. The longest follow-up is two and one-half years. After this period of time the graft remains less opaque than the surrounding bone but provides excellent contour and function.

SUMMARY

The repair of cranial defects with fresh autogenous iliac bone is an excellent method of cranioplasty. The procedure is indicated for repairing large defects of the cranium and in reconstruction where contouring is essential. It is to be preferred over other methods because it is physiologically sound, it is readily available in adequate quantity, contouring is easy, slipping and springing of the graft do not occur, and air or arteriographic studies can still be visualized. In addition, foreign body reaction and infections are probably less likely to occur. The technique of obtaining, shaping, and fitting the graft is described in detail.

FURTHER OBSERVATIONS UPON INTRAMEDULLARY PRESSURES DURING THE FIXATION OF FRACTURES BY KÜNTSCHER'S[1] METHOD

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INTRODUCTION

IT HAS been demonstrated that a considerable transient rise in pressure accompanies the insertion of an intramedullary nail into a long bone in the manner used to fix fractures.[3] This rise in the intramedullary pressure is closely related to the design of the nail employed, being greatest with nails of solid construction. The possible dangers associated with this rise in pressure, i.e., fat and parenchymatous embolism, have been pointed out.[3, 4] The initial experiments were carried out upon human tibiae which were intact, not fractured. It was felt that the principles demonstrated in the intact bones could be applied to fractured bones in greater or lesser degree, depending upon the position and configuration of the fracture, and the operative technique. Nevertheless, an objection has been raised, that the data obtained using unfractured tibiae were not germane to the clinical application of intramedullary nailing in fractures.[2] Therefore, further measurements of intramedullary pressures in fractured bones have been made.

METHOD

Four human tibiae were obtained from fresh amputation specimens. One was kept intact as a control. Transverse fractures were produced in two, a spiral fracture in another. The fractures were reduced as at operation and held in position with clamps. The superior tibial plates just anterior to the tibial spines were perforated with a drill to allow insertion of intramedullary nails of cloverleaf design. The nails were driven the full length of the shafts by means of blows from a light hammer. The increase in intramedullary pressure arising during the insertion of the nails was measured continuously by electrically recording strain gauges attached to three No. 5 needles, inserted into the medullary cavity through holes drilled in the cortex at the junction of the upper and middle thirds, the junction of the middle and lower thirds, and at the mid-point of the shaft (Fig. 1). The entire experiment was carried out with the bones at 37° C., so that the fatty marrow would have its normal fluidity.

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*Fellow of the National Foundation for Infantile Paralysis.

RESULTS

The method of continuously recording the intramedullary pressures demonstrated two interesting phenomena. The pressure peak accompanies the tip of the nail down the intramedullary cavity as shown in the accompanying diagram (Fig. 1). The time interval between hammer blows greatly affects the maximum pressure attained. If the blows follow quickly, one upon the other, the rises in pressure associated with each blow fuse, and in summation far exceed the individual increments. The summation is minimal when the blows are separated by 30 seconds or more. The duration of the increased intramedullary pressure is relatively short, the pressure returning to within normal 60 seconds after the last hammer blow. The highest pressure recorded

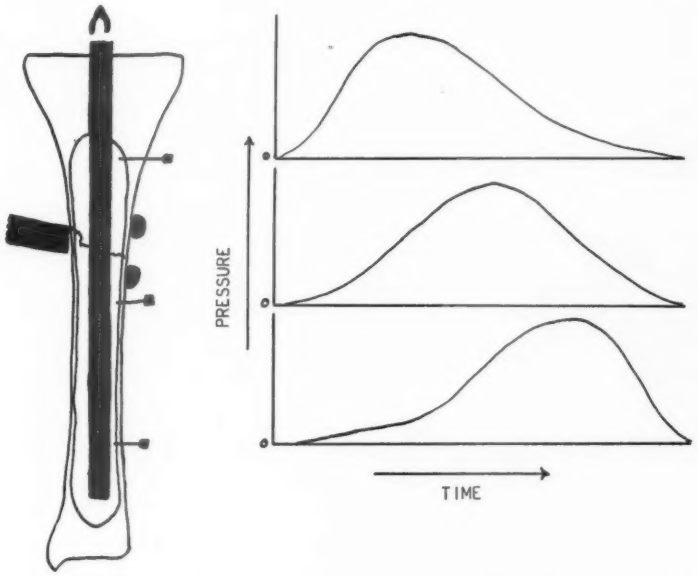

Fig. 1.—Diagram illustrating the method of study and the progress of the pressure peak down the medullary cavity as the nail is inserted. This peak may reach as high as 380 mm. Hg.

was 380 mm. Hg in the specimen with a transverse fracture through the middle third. Maximum pressures of 240, 250, and 180 mm. Hg were recorded in the other specimens. These maximum pressures were of short duration, i.e., 10 to 20 seconds, but the period of increased intramedullary pressure extended throughout the process of inserting the nail. The presence of the fractures did not appear to affect the rise in intramedullary pressure.

DISCUSSION

The possible consequences of a transient rise in the intramedullary pressure during intramedullary nailing have been discussed elsewhere.[3, 4] The movement of the marrow displaced by the nail is accomplished by this increase in pressure. Using the continuous method of recording pressures, the summation of the effects of successive hammer blows, as well as the movement of the pressure peak down the intramedullary cavity can be demonstrated.

The differences between the maximum pressures recorded by the strain gauges and those recorded by the capillary mercury manometers used previously can be explained by the greater sensitivity of the former. It can be seen that the insertion of an intramedullary nail into a fractured long bone, reduced and held in position by a clamp, produced changes in the intramedullary pressure essentially similar to those demonstrated to occur in intact bones. The explanation of this behavior is twofold: (1) The accurate coaptation of the fragments firmly held by a clamp produces an effective seal and therefore an essentially intact bone; and (2) the distal fragment, if the nail fills the medullary canal as it should, is a shorter model of the whole, intact bone.

CONCLUSIONS

1. The insertion of an intramedullary nail into a fractured long bone produces a rise in the intramedullary pressure of considerable magnitude.

2. This rise in pressure persists throughout the period of insertion.

3. The maximum pressure is greatest when the hammer blows are close together and summation occurs.

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SCRUBBING THE PLEURA IN THE TREATMENT OF CHRONIC AND RECURRENT SPONTANEOUS PNEUMOTHORAX

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EVERY general hospital should be familiar with the treatment of spontaneous pneumothorax. This should embrace not only decompression procedures for the relief of tension, but also a knowledge of the more troublesome chronic and recurrent types of the disease. During the past ten years, thirty-eight cases of nontuberculous spontaneous pneumothorax have been admitted to the Rhode Island Hospital and the three deaths which occurred in this series can be attributed to lack of proper treatment.

Fortunately, most cases of spontaneous pneumothorax require little in the way of therapy. The lung expands in a relatively short time without recurrence of collapse or other undesirable sequelae. Our chief concern is with those cases in which the lung fails to expand or in which collapse continues to recur over a varying period of time. These present a real problem and various methods of treatment have been suggested.

In 1939, Hennell and Sternberg[11] wrote, "Once a chronic state has been established, a cure will not occur unless a more vigorous inflammatory pleural reaction intervenes and brings about the sealing of the chronic, partially epithelized pleuropulmonary communication." This suggested the indication for chemical pleuritis. Spengler first conceived the idea in 1901, and a few years later suggested the use of 0.5 per cent silver nitrate solution as the chemical irritant. By 1914 he had forsaken silver nitrate for 30 per cent dextrose, reporting the first case in 1923. Since that time, reports confirming or denying the efficacy of a chemical irritant have invaded the literature. Silver nitrate and hypertonic glucose solutions have been added as well as talcum powder, iodine, hypertonic saline, iodoform, many oils, and the patient's own blood. Inconclusive results of such therapy suggest the need of a more satisfactory method, and many authors are of the opinion that the surgical approach is frequently more practicable.

Brewer, Dolley, and Evans,[3] in 1950, cited only twenty cases from the literature of surgical therapy, twelve of which were reported in the 1948-1949 period.

Phrenic paralysis, to relax the diaphragm and decrease tension on the lung to encourage healing of the fistula, has been attempted. Thoracoscopy with lysis of adhesions has also been tried. However, thoracotomy associated with a definitive procedure seems to have given the most satisfactory results. These have varied from the simple lysis of pleural adhesions to lobectomy or pneumonectomy for the removal of large air cysts associated with pneumothorax. When a bronchopleural fistulous tract has been apparent, it has been

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closed with simple sutures. Excision of a solitary cyst or bleb and decortication of the lung to remove a thickened visceral pleura has also been performed. Niehaus[18] reported a case in 1947 in which he actually sutured the visceral pleura to the chest wall.

Recently Davenport[8] reported the successful use of forced suction aspiration in nineteen cases of spontaneous pneumothorax in tuberculous patients. This technique was applied chiefly to the early rather than to the chronic, type of pneumothorax.

Failure of the lung to expand may be attributed to two factors. During the early phase, a bronchopleural fistula is present which may become sealed and allow for early and uneventful recovery, or it may remain open for a more prolonged period, in which case the collapsed lung tends to become adherent to the adjacent parietal pleura and covered with a thin layer of filmy adhesions which prevent re-expansion even after closure of the fistula. The other alternative is repeated opening and closure of the fistula which allows for an alternate collapse and expansion of the lung—recurring spontaneous pneumothorax.

In the chronic pneumothorax case, the presence or absence of a fistula can be demonstrated easily at the time of operation. When positive pressure is applied by the anesthetist, air can be heard escaping from the fistula. If localization is difficult, the pleural cavity is partially filled with fluid and the site from which the bubbles arise indicates the fistulous tract. If the lung has been collapsed for a period of months, it is impossible to expand it with positive pressure even in the absence of a fistula because of the fibrous tissue envelope which surrounds it. This illustrates the futility of conservative methods of treatment, and the absolute necessity for decortication of the entire lung surface.

The chronic recurring type of spontaneous pneumothorax presents a somewhat different problem. Surface adhesions are of less importance and usually are not sufficient to prevent the lung from expanding. Recurring episodes of chest pain and dyspnea are its outstanding features, often without definite localization of the offending side by the patient. The constant threat of tension pneumothorax always hangs over cases of this type.

Case 1, a patient who left the hospital after having had a spontaneous pneumothorax with re-expansion, was readmitted in extremis two months later. The mistake was made of aspirating the side for which he had previously been treated, and he died shortly after admission of tension pneumothorax on the opposite side.

Case 3, a patient who had had a history of spontaneous pneumothorax for a period of three years, and was admitted for surgery of the right chest, developed a spontaneous pneumothorax on the left side on the fifth postoperative day. The patient himself had never been able definitely to localize his symptoms to either the right or the left chest, and all previous x-rays had revealed a right pneumothorax.

Recent reports in the literature indicate that there is now a greater appreciation for open surgical treatment in chronic and recurring pneumothorax. The operation, which consists merely in opening the thorax and dealing with the lung surface, is a comparatively minor procedure and should carry with it no mortality. It is surprising that recent comprehensive reports[3, 4, 16] made no mention of employing a method which insures the formation of adhesions between the visceral and parietal pleura in order to avoid recurrence of the condition. Regardless of etiology, this should be the fundamental aim of any method of treatment. The resection of a bleb where a leak has occurred is no insurance against recurrence. Blebs are frequently present in various parts of the lung surface, and, in many instances, in great numbers. Each is a potential hazard, yet excision and closure of a large number of small blebs is impracticable, and, if carried out, does not in itself prevent recurrence.

In the cases to be reported we have employed, in addition to resection of blebs when they are of significant size, decortication of the lung surface and have made it a point to scrub the entire visceral and parietal pleura with rough gauze in order to create an inflammatory reaction on all its surfaces. This has resulted in the early formation of a serosanguineous exudate, following which, early aspiration is carried out to allow the visceral and parietal pleura to become approximated with the formation of firm adhesions. In certain instances, catheter suction may seem to be desirable, especially where prolonged collapse has resulted in a diminished lung volume. Either method should ensure success, although in the latter infection is more prone to occur.

The first mention in available literature of wiping the pleura with gauze is difficult to ascertain. Its primary use stemmed from the progress of the two-stage lobectomy, when it was considered that, for a safe lung resection, the ideal combination was a firmly adherent healthy lobe and a free diseased one. Lilienthal,[14] in his 1925 edition of *Thoracic Surgery,* suggested as one method of accomplishing the desired result: "Roughen the healthy visceral and parietal pleura with gauze and then paint the surface with tincture of iodine." Churchill[5] when discussing the two-stage lobectomy in 1937 stated, "The parietal pleura is now scrubbed briskly with dry gauze over the anterolateral aspect and the costovertebral gutter to promote adhesions with the upper lobe." He claimed that adhesions resulting from the trauma introduced at the first stage operation are invariably light and usually nonvascular.

Tyson and Crandall,[23] in 1941, also mentioned that pleural adhesions can be more certainly attained by rubbing the pleural surface with gauze and reexpanding the lung at the close of the operation. In reviewing the literature, we find in a personal communication cited by Tyson and Crandall,[23] that Churchill explored the pleural cavity in search of a valve vesicle, and being unable to locate the site of the fistula, roughened the pleura with gauze with a satisfactory postoperative result. This conceivably may be our first indication of such a procedure being performed for this condition. This previous, yet coincidental, therapy became known to us only in our search of the literature, following its use by us in the cases to be presented in this paper.

It suggested itself to us because during the earlier days of pulmonary resection, the two-stage lobectomy was an accepted and widely used procedure. At that time, scrubbing of the pleura was done more or less routinely and contributed considerably to the improved results of tourniquet lobectomy, in which the presence of a bronchopleural fistula and an associated collapsed healthy lobe was a serious and not uncommon complication.

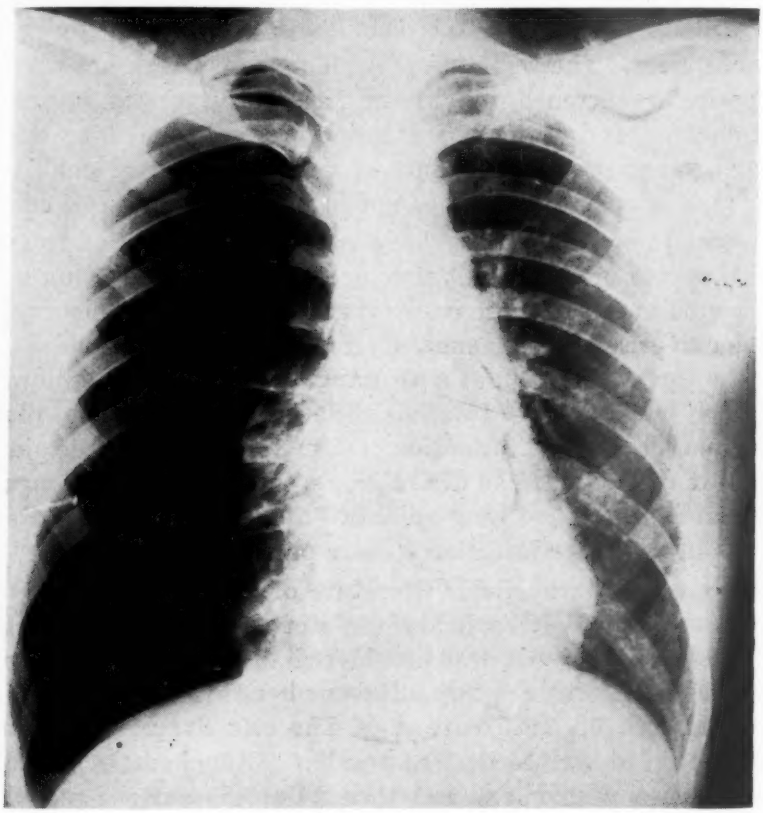

Fig. 1 (Case 1).—Right pneumothorax. This patient died later from a left tension pneumothorax.

CASE 1.—M. M., a 27-year-old white man, entered Rhode Island Hospital on Jan. 6, 1946, complaining of a productive cough of five weeks' duration. This was associated with pain in the right shoulder and there was some pain in the left chest. He gave no history of dyspnea. The positive physical findings were limited to the chest. There was bulging of the right thorax posteriorly, hyperresonance and absent breath sounds. The left chest was essentially normal.

The admission laboratory findings included a white blood count of 15,300 and a hemoglobin of 17.2 Gm. The clinical impression of right pneumothorax was verified by a chest x-ray which showed complete collapse of the right lung with slight herniation of the mediastinum to the left. The left lung showed exaggeration of perivascular markings.

The patient was given bed rest and 900 c.c. of air were removed from the right pleural cavity. The patient became symptom-free and was discharged on the twelfth hospital day, although his lung was only partially expanded.

Second Admission.—The patient was brought to the accident room on March 3, 1946, in a state of severe respiratory distress. One hour prior to admission he had become acutely ill

with severe dyspnea and cyanosis. His respirations were very shallow, with a rate of four per minute. The diagnosis of tension pneumothorax was made and a needle was immediately introduced into the right pleural cavity with no relief of symptoms. The patient died within a few minutes.

A post-mortem examination revealed congenital polycystic disease of both lungs with involvement of all lobes and a total pneumothorax on the left side. There was no pneumothorax on the right side, but there was a mild inflammatory reaction of the pleura attributed to the recent pneumothorax episode. The lobes of both lungs were honeycombed with cystic cavities measuring up to 2 cm. in diameter.

CASE 2.—L. W., a 16-year-old white youth, entered Rhode Island Hospital on Aug. 8, 1949. Three hours prior to admission, following strenuous exercise, the patient was seized with a sharp, tearing pain in the right anterior chest, and dyspnea. At the time of admission, these symptoms had diminished in severity.

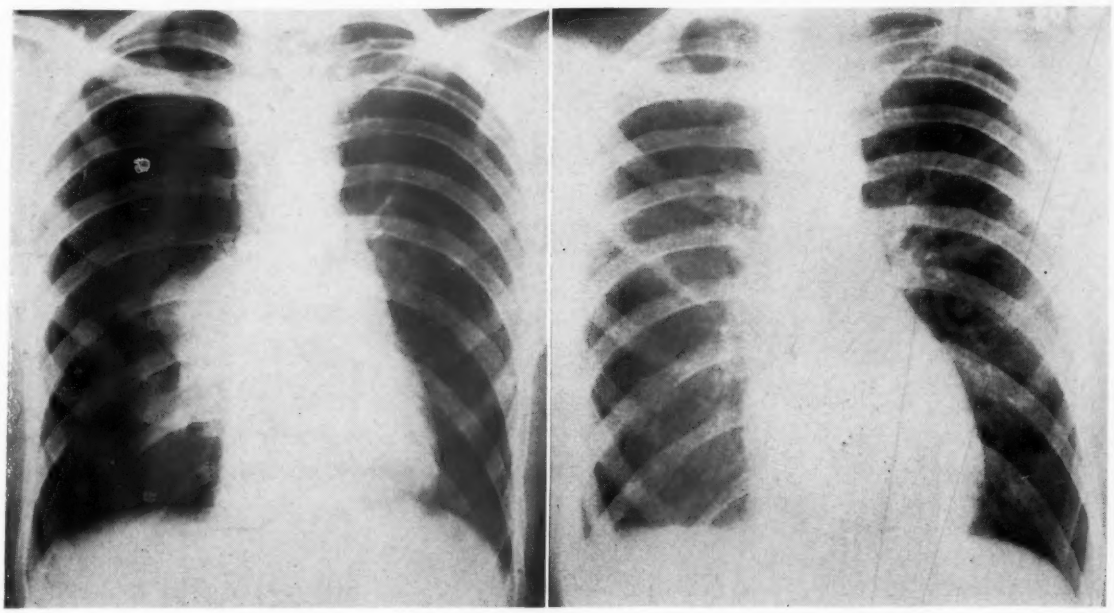

Fig. 2. Fig. 3.

Fig. 2 (Case 2).—Almost total collapse of right lung.
Fig. 3 (Case 2).—Complete expansion of lung following surgery.

Physical examination revealed a young man with anxious facies and shallow, rapid respirations. Examination of the chest revealed absent tactile and vocal fremitus over the right hemithorax with hyperresonance and absent breath sounds. The coin test sign was positive. X-ray of the chest on admission showed a total collapse of the entire right lung with slight shifting of the mediastinum toward the left. When the patient was given bed rest, the lung expanded about 50 per cent, but this was followed by complete collapse four days later.

Because the patient's lung showed no tendency to expand after thirty-seven days of observation, surgery was decided upon. The right pleural cavity was opened through the sixth intercostal space and the lung was found to be completely collapsed. On the anterior surface of the upper lobe, several bullae were noted, the largest of which was 2.5 cm. in diameter. Positive pressure was instituted by the anesthetist and a definite leak was immediately demonstrated on the posterior surface of the middle lobe. The air was seen to escape from a large bulla which was attached to the posterior chest wall by thin fibrous adhesions. This segment

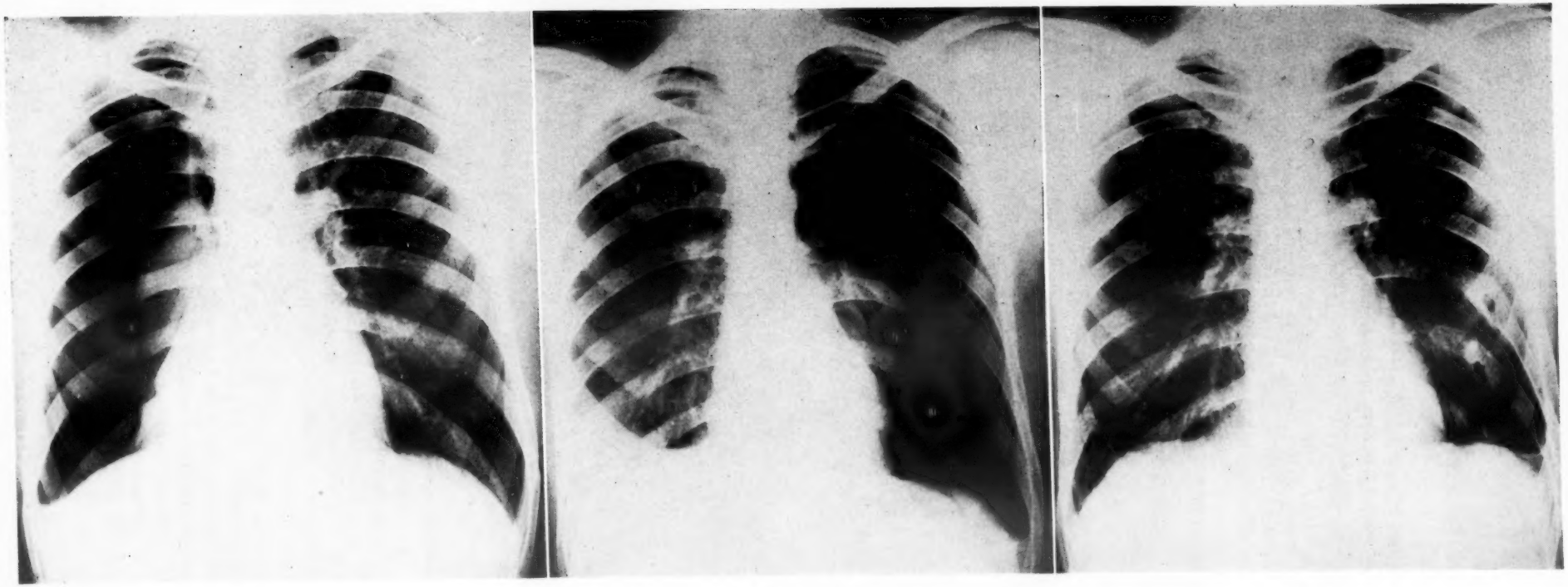

Fig. 4.

Fig. 5.

Fig. 6.

Fig. 4 (Case 3).—Recurring right spontaneous pneumothorax prior to operation.
Fig. 5 (Case 3).—Operation has been performed on the right side. Note residual pleural exudate and the almost total collapse of the left lung.
Fig. 6 (Case 3).—Roentgenogram taken seventeen months after surgery on right chest and fifteen months following operation on left chest.

of lung was excised and the lung closed with mattress sutures of No. 0000 silk. All surfaces of the visceral and parietal pleura were then scrubbed with rough gauze to create an inflammatory reaction. The pleural cavity was closed without drainage. The patient made an uneventful recovery from the operation and developed a pleural effusion which was aspirated on the sixth postoperative day with the removal of 250 c.c. of serosanguineous fluid. A subsequent tap on the tenth postoperative day produced only 10 c.c. of the same type of fluid.

He was discharged on the fourteenth postoperative day with complete re-expansion of the right lung. He has been followed for nineteen months and has been completely symptom-free with no further episodes of spontaneous pneumothorax.

CASE 3.—A. A., a 21-year-old white man, entered the Rhode Island Hospital on July 18, 1949, complaining of shortness of breath of one week's duration. He stated that he had had many similar episodes during the past three years. Three months prior to admission, the diagnosis of right spontaneous pneumothorax was made for the first time and confirmed by x-ray. He was admitted to the Medical Service where an attempt was made to obliterate the pleural space with hypertonic glucose solution. The degree of collapse as seen by x-ray was about 50 per cent. On July 19, 1949, 50 c.c. of 50 per cent glucose solution were introduced into the right pleural cavity. This apparently had very little effect, for no pleural exudate developed. Five days later, 30 c.c. of 67 per cent glucose were introduced. The patient was discharged on the following day, his lung having expanded to 90 per cent of normal, but with no evidence of a pleural reaction.

Second Admission.—During the three-week interval between the first and second admission, the patient was carefully followed and had another episode of spontaneous pneumothorax with the lung dropping down to about 60 per cent of normal. Because of repeated episodes of dyspnea which had occurred during the past three years, the patient had become quite apprehensive and was willing to submit to surgical intervention which was recommended at this time. On Aug. 17, 1949, the right pleural cavity was explored through the sixth intercostal space. A thin-walled bleb measuring 2 by 1.5 cm. was present on the apical portion of the upper lobe. At its base was a bandlike adhesion 2 cm. in length and 1.5 cm. in width, which was attached to the posterior chest wall. Another, smaller bleb was present on the anterior surface of the upper lobe. The larger bleb and the adjacent lung tissue were resected and the defect closed with mattress sutures of No. 000 catgut. The smaller bleb was obliterated with a mattress suture. Positive pressure by the anesthetist was then made and the lung was partially expanded, but no additional blebs were noted. No further pressure was made upon the lung in order to avoid undue stress upon the suture lines. The entire visceral and parietal pleura were scrubbed vigorously, after which the chest wall was closed without drainage.

The patient made an uneventful recovery and was discharged on the eleventh postoperative day. The usual pleural effusion developed which required aspiration on the sixth postoperative day with the removal of 400 c.c. of serosanguineous fluid. X-ray taken on the seventh day after operation, in addition to demonstrating the pleural effusion on the right side, revealed almost complete collapse of the left lung (Fig. 5). This was our first knowledge that we were dealing with a case of bilateral spontaneous pneumothorax. The fact that the pneumothorax on the left side had developed without symptoms raised the question of whether or not it had occurred during the course of the recent operation. The patient was advised that he should return for a similar operation on the left chest, to which he agreed.

Third Admission.—Following discharge from the hospital, the patient had definite symptoms of spontaneous pneumothorax on the left side. These episodes, although not severe, were confirmed by ambulatory fluoroscopy. An x-ray taken immediately upon the third admission on Oct. 3, 1949, revealed a 50 per cent collapse of the left lung. The pleural effusion on the right had completely absorbed and there was slight haziness indicating some pleural thickening.

The left pleural cavity was explored on Oct. 4, 1949. There was a cluster of several small blebs on the apical portion of the upper lobe as well as minute areas of blebs on all surfaces of this lobe, measuring from 2 to 5 mm. Endotracheal pressure was increased by the anesthetist and, although a small escape of air could be heard, it was difficult to localize the point of rupture. Saline solution was introduced into the pleural cavity. Small bubbles of air were seen to arise from the apical portion of the upper lobe where the cluster of small blebs had been noted. A small segment was then removed in this area and the lung closed with interrupted mattress sutures of No. 000 chromic catgut. The entire visceral and parietal pleura were then scrubbed with gauze until a sanguineous ooze developed, after which the chest was closed with a No. 24 catheter in the seventh intercostal space for suction. It was removed on the sixth postoperative day, at which time the left lung was completely expanded.

The patient was discharged from the hospital on the ninth day following operation. It was necessary to readmit him two weeks later on Oct. 31, 1949, because of a loculated empyema at the site of the catheter. Thoracotomy with rib resection was carried out with prompt relief of symptoms. He was followed for seventeen months with no recurrence of pneumothorax on either side.

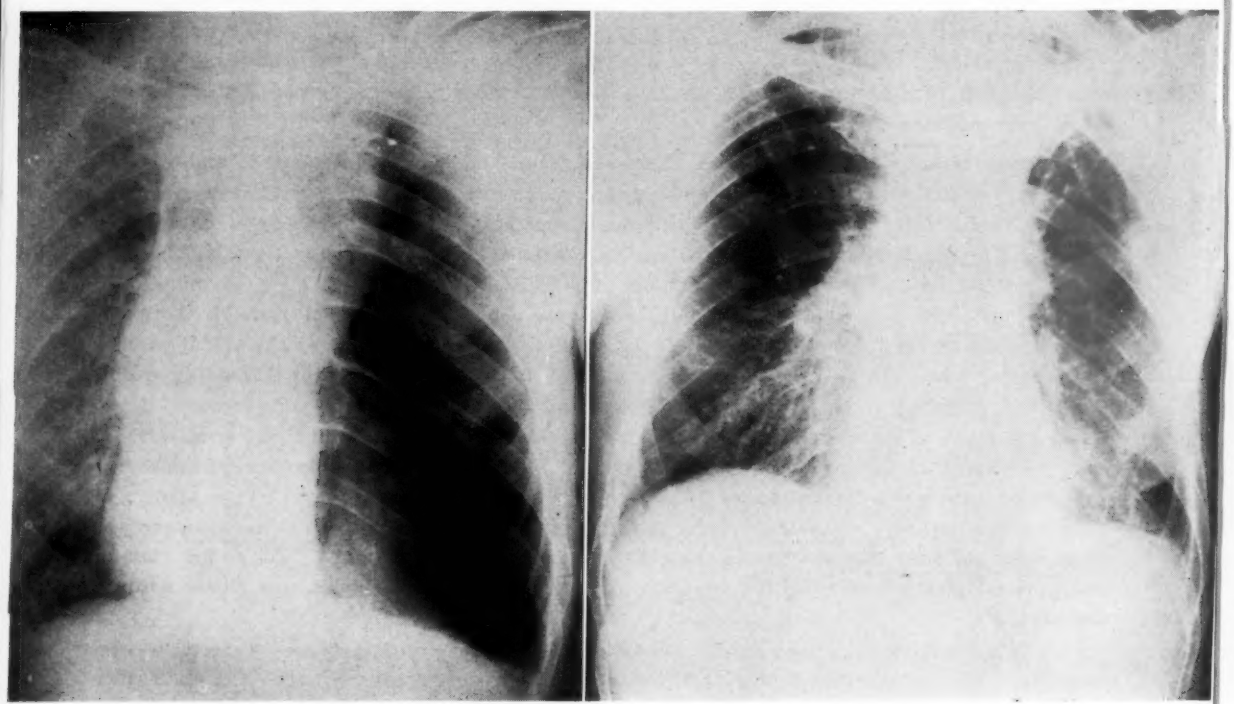

Fig. 7. Fig. 8.

Fig. 7 (Case 4).—Chronic left pneumothorax of nine months' duration.
Fig. 8 (Case 4).—Pleural space has been completely obliterated postoperatively.

CASE 4.—M. A. O., a 63-year-old white man, entered the Rhode Island Hospital on Sept. 25, 1950, with a chief complaint of dyspnea of nine months' duration. The illness was initiated by a sudden and violent paroxysm of coughing which recurred frequently during the next few days.

Dyspnea had been a prominent and distressing symptom making it impossible for him to walk more than 100 feet without resting.

He was referred by his family physician for an x-ray of the chest which showed a total pneumothorax on the left side. Several repeat chest x-rays were taken during the course of

the nine months prior to admission, but no change was noted and at no time was there any evidence of partial expansion of the lung. He was finally referred to the Thoracic Clinic at the Rhode Island Hospital where admission was advised.

Physical examination revealed a healthy white man lying quietly in bed in no apparent distress. All significant findings were limited to the thorax. The trachea was displaced to the right. The hemithorax showed marked hyperresonance, absence of breath sounds, tactile and vocal fremitus. An x-ray at this time confirmed the diagnosis of a total collapse of the left lung with the heart and mediastinum displaced to the right.

Operation was performed on Sept. 30, 1950. The left lung was completely collapsed into the paravertebral gutter, where it was fixed by firm adhesions, and in addition the surface of the lung was covered with thin filmy adhesions. There was a broad band 5 cm. in length and 1 cm. in width running from the apex of the upper lobe to the adjacent posterolateral parietal pleura. The lung in this area showed definite evidence of parenchymal disease with an area of scarring 2.5 cm. in diameter. Gross examination suggested chronic tuberculosis as the most probable etiology. The entire lung was mobilized from all its pleural attachments to the chest wall and mediastinal pleura after which positive pressure was applied by the anesthetist. The lung expanded to only about one-third of its volume and was seen to be held down by a thin layer of adhesions over its entire surface. Complete decortication of the lung was performed until it was possible to expand it to about 90 per cent of its volume. The entire visceral and parietal pleura were then scrubbed vigorously with dry gauze and the chest wall closed with one No. 20 catheter in the ninth intercostal space in the posterior axillary line for dependent drainage. Two No. 20 catheters were also inserted in the upper third of the chest, anteriorly and posteriorly, and placed on 12 cm. of water suction when the patient was returned to the ward.

The patient made an uneventful recovery and on Oct. 12, 1950, an x-ray revealed a 15 per cent pneumothorax on the left side. On October 13, the posterior catheter was removed and the catheter opening in the chest wall closed with a single silk suture. Complete expansion of the lung occurred more slowly after this point than in Cases 2 and 3. This was attributed to the contracture of the lung from the total and prolonged collapse. For this reason, the removal of the second catheter was delayed until the fifteenth postoperative day. Considerable pleural exudate developed in loculated spaces which required repeated aspirations at various points with removal of serosanguineous fluid varying in quantity from 25 c.c. to 200 c.c.

He was discharged on Nov. 3, 1950, at which time there was still a slight residual pneumothorax at the apex of the chest with moderate haziness due to thickened pleura. The lung was obviously firmly attached to the chest wall except at the apex, and it was felt that the expansion would be completed by an obliterative pleuritis. The patient was seen in the Thoracic Clinic on Jan. 4, 1951, at which time x-ray examination showed that expansion was complete.

The outstanding feature of this patient's postoperative course was the dramatic relief from dyspnea which occurred a few days following operation. Since surgery, he has remained free of symptoms and has resumed normal activity.

SUMMARY AND CONCLUSIONS

In chronic and recurring spontaneous pneumothorax, open surgical treatment would seem the most satisfactory and definitive method of obtaining permanent cure.

It is suggested that thorough scrubbing of the visceral and parietal pleura with rough gauze results in the formation of firm adhesions between these two surfaces making recurrence impossible.

When dealing with recurring pneumothorax where the lung tends to re-expand readily and fill the pleural cavity, it is more desirable to close the

chest without drainage. The pleural exudate, which invariably develops, is removed by needle aspiration to allow the pleural surfaces to become adherent.

The treatment of chronic pneumothorax should include, in addition to scrubbing the pleura, a careful and complete decortication of the lung, and the pleural cavity should be placed on suction. This seems necessary to facilitate the obliteration of the pleural space when diminished lung volume has been present over a prolonged period.

Four operations have been performed on three patients with chronic or recurrent spontaneous pneumothorax who had failed to respond to conservative therapy. The technique and the results are presented.

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ARSENICAL EPITHELIOMAS OF MEDICINAL ORIGIN

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INTRODUCTION

THAT certain arsenic compounds are effective carcinogenic agents has been well documented by the occurrence of cutaneous epitheliomas in persons with occupational and environmental exposure to this element.[1, 3, 5, 6, 15, 16, 26] Also there are reports of the successful use of arsenic in tumorigenesis in laboratory animals.[11, 24, 25] Although there has been considerable literature reporting the induction of cancers by arsenic in its various medicinal forms, use of this carcinogen in therapeutics has not ceased. For this reason, it seems desirable to continue reporting cases of arsenical epithelioma and again to point out this unfortunate and almost wholly preventable type of malignancy.

While this is a report of arsenical cancers of medicinal origin, the broader occupational and environmental exposure to arsenic should be mentioned. Since the time of Paris' original report (1820)[21, 22] of cutaneous malignancy among the workers in the copper smelters and foundries of Cornwall, innumerable industrial exposures to arsenic have developed. Epitheliomas have been reported secondary to the handling of sheep-dip and the mining of silver and copper. They have developed among workers in the vineyards of Germany, and as the result of the use of arsenical sprays in agriculture, forestry, and horticulture.[1, 3, 6, 15, 16, 23] Epitheliomas and chronic arsenism due to environmental exposure has been demonstrated by the historic episodes in Reichenstein, Silesia. Here gold, silver, and arsenic mining operations for centuries have resulted in contamination of spring water by large spoil banks containing arsenical wastes. So-called Reichenstein's disease, characterized by chronic arsenism with its neuritis, and its gastrointestinal, hepatic, and cutaneous manifestations, was comprehensively reported by Geyer.[7] More recently, reports from Argentina by Arguello[2] describe arsenical keratoses and epitheliomas resulting from contaminated drinking water and foodstuffs. It is perhaps impossible to presently estimate our real or potential environmental exposure to arsenic. However, the United States as the largest user and producer of arsenicals such as insecticides and parasiticides in agriculture and forestry has an increasing potential occurrence of environmental arsenism among its population.

As early as 1885 White[28] described the sequence of "psoriasis, verruca and epithelioma" in 2 patients who had received arsenic as treatment for psoriasis.

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He mentioned a similar case of psoriasis followed by palmar and plantar keratoses described by Dr. Cartay in 1878 in the Gazette des hôpitaux civils et militaires but failed to suspect arsenic as a possible etiological agent. The medicinal origin of arsenical epitheliomas was first described by Hutchinson in 1887.[10] Hutchinson attributed the keratoses and epitheliomas occurring in patients with psoriasis to the arsenic contained in the Fowler's solution (potassium arsenite) used for treatment. He considered White's cases as due to the same etiological agent. This observation has been confirmed by many subsequent investigators.[5, 8, 17, 26] Hueper[9] placed the total number of reported cases of medicinal arsenical epitheliomas as approximately 115 from 32 reports published prior to 1942. Inorganic trivalent or pentavalent arsenic compounds such as potassium arsenite contained in Fowler's solution, arsenic tri-iodide contained in Donovan's solution, are the principal etiological agents, although there are infrequent and questionable reports of the occurrence of cutaneous malignancy attributed to the therapeutic use of organic arsenicals (arsphenamines and cacodylates).[3, 12] Cutaneous malignancy has occurred where the inorganic arsenic compounds have been used in the symptomatic treatment of psoriasis, bronchial asthma, rheumatism, chorea, polycythemia, leucemia, migraine epilepsy, chronic eczema, various psychoneuroses, or as a general tonic. However, arsenical epithelioma has been an extremely rare complication of antiluetic, organic arsenical therapy.

The purpose of this study is to report 8 cases of cutaneous malignancy of medicinal arsenical origin encountered in the Tumor Clinic of the University of Minnesota Hospitals during a two-year period. One case of benign superficial epitheliomatosis observed at the Fort Snelling Veterans Administration Hospital has been added to this report.*

In view of the relatively few total cases reported, the finding of 8 new cases in 2 years in a tumor clinic that has seen 110 new cases of skin cancer during this period suggests that the disease is found to be relatively common if one is aware of its occurrence and manifestations and searches diligently through his material.

DIAGNOSIS

The diagnosis of arsenical epithelioma is a composite one depending upon the cutaneous manifestations of chronic arsenism and a positive history of exposure to medicinal arsenic. Additional supportive evidence includes the demonstration of arsenic in the lesions either by quantitative chemical or histochemical means[14, 17, 20] and, less importantly, the exhibition of arsenic in hair, nails, and urine.

The cutaneous manifestations of chronic arsenism which may precede arsenical skin cancer are: (1) disturbances of pigmentation, i.e., hyperpigmentation or melanosis, and (2) keratoses. Hyperpigmentation, usually a grayish brown to deep brown or black color, occurs most commonly in sites which are normally more pigmented than the adjacent skin, e.g., the areola, axillae, groin, perineum, and in areas exposed to pressure or friction such as the belt line.

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Mottled patches, areas of melanosis adjacent to areas of leucoderma are often seen. The keratoses are the most noteworthy features associated with occupational as well as nonoccupational arsenical exposure. Early, these lesions have a roughened, sandpaper-like feel. Later they may become fissured or wartlike with stalactite-like horns occurring most commonly on the palms or soles. Their precancerous nature is well recognized. On the hands they frequently occupy the lateral borders, thenar eminence, and the backs of the fingers, especially over the phalangeal joints. However, keratoses may be found on any part of the skin surface. They may remain stationary, or regress, or may exhibit progressive growth to finally assume malignant character. The malignant lesions characteristically assume the gross features of the different types of cutaneous epithelioma (squamous-cell, basal-cell, and mixed-cell types). Occasionally they may assume the superficial plaquelike forms simulating the lesions of superficial epitheliomatosis. Other lesions may be indistinguishable from the appearance of Bowen's intraepithelial epitheliomatosis. Not uncommonly the different types of epithelial neoplasms coexist in the same individual. There is a division of opinion as to whether Bowen's disease and so-called benign superficial epitheliomatosis are due to arsenic.[1, 3, 14, 19]

Through its properties as a metabolic and capillary poison, arsenic may affect many organs. Careful interrogation of the patient may reveal additional signs and symptoms of arsenism reflecting effects on other systems. The noncutaneous manifestations include central and peripheral disorders of the nervous system; hematopoietic disturbances—usually a microcytic anemia; chronic respiratory disturbances such as pharyngitis, bronchitis, and occasionally perforation of the nasal septum; and alimentary disorders—gastrointestinal symptoms during the acute stage, cirrhosis of the liver latently.

DISCUSSION

Although critical analysis of the incidence of arsenical epithelioma is not available from the reports thus far, a relative estimate of frequency can be made from the fact that 8 new cases were diagnosed among 110 cases of cutaneous malignancy seen in our tumor clinic during a two-year period. In 5 of the cases the correct diagnosis was made during the first visit to the clinic. The additional 3 cases were found by rechecking the records of new cases of skin cancer for items that might suggest arsenic as a possible etiological agent. Reexamination and interrogation of 31 such suspects revealed 3 cases of arsenical epithelioma. In the light of these observations it is suggested that careful questioning of all patients with cutaneous malignancy for previous exposure to medicinal arsenic occurring in association with chronic arsenical dermatosis, especially palmar and plantar keratoses, and less importantly, disturbances of pigmentation, nail and hair growth, will result in an increased frequency of a diagnosis of arsenical epithelioma. Although there are too few cases for a valid statistical study, it is interesting to analyze certain aspects of the cases where data are complete regarding the dosage of arsenic, duration of therapy, and length of latent period between exposure and onset of lesions. In the cases

TABLE I. ARSENICAL EPITHELIOMAS OF MEDICINAL ORIGIN: PROTOCOL OF CASES

CASE AGE SEX	EXPOSURE TO MEDICINAL ARSENIC	ARSENICAL EPITHELIOMAS	OTHER MANIFESTATIONS OF CHRONIC ARSENICAL DERMATOSIS	INTERVAL BETWEEN EXPOSURE AND ONSET OF LESIONS	TREATMENT	COURSE AND DURATION OF DISEASE
1. P. R. 50 M	Received potassium arsenite (Fowler's solution), 6 to 20 drops daily, from the age of 25 to 28 years as treatment for bronchial asthma	1. Squamous-cell carcinoma of right medial malleolus (5 by 5 by 1 cm.) 2. Basal-cell carcinoma of neck	Multiple hyperkeratoses of both palms and soles, numerous hyperkeratoses and patchy hyperpigmentation of the trunk	Keratoses—3 years Epithelioma—"about 19 years"	Supracondylar amputation right lower extremity and radical right inguinal lymph node dissection (nodes negative for metastases); x-ray therapy of basal-cell carcinoma of neck; electrodessication of multiple hyperkeratoses	No evidence of recurrence or metastases 2 years after treatment
2. F. P. 51 F	Received Fowler's solution, 10 to 15 drops daily, for 6 months at the age of 15 years, as treatment for Sydenham's chorea and rheumatic fever	1. Squamous-cell carcinoma right index finger (2.5 by 1 by .5 cm.) 2. Squamous-cell carcinoma of dorsum of left hand 3. Two small squamous-cell carcinomas of right ankle and one of left ankle	Multiple punctate hyperkeratoses of palms and soles, hyperpigmented areas and keratoses of the legs	Keratoses—1 year First epithelioma—"about 28 years"	Amputation of right index finger, and wide excision of all other epitheliomas; electrodessiccation of palmar and plantar keratoses	Keratoses present 35 years and epithelioma present 7 to 8 years prior to surgical treatment; no recurrence or metastases after 6 months
3. G. S. 66 M	Received Fowler's solution daily for 12 months as treatment for psoriasis at the age of 25 years	1. Squamous-cell carcinoma, right 5th finger (1 by 2 by .5 cm.)	Multiple palmar and plantar hyperkeratoses and cutaneous horns; flat keratoses of trunk with widespread brownish mottling of the skin	Keratoses—"about 26 years" Epithelioma—"about 39 years"	Amputation of right 5th finger with radical right axillary lymph node dissection (all nodes negative for metastases); local excision of 3 largest keratoses and electrodesiccation of others	Duration prior to treatment: keratoses—15 years, epithelioma—2 years; no recurrence of epithelioma or metastases 1 year after surgery; continues to develop new palmar and plantar keratoses
4. W. G.	Took Fowler's solu-	1. Squamous-cell car-	Multiple palmar and	Not known	Amputation of right	Duration prior to

4. W. G. pharmacist 78 M	Took Fowler's solution as a general tonic intermittently for many years	1. Squamous-cell carcinoma of right thumb 2. Squamous-cell carcinoma of right infraorbital area	Multiple palmar and plantar keratoses with flat keratoses and hyperpigmented areas on dorsum of hands	Not known	Amputation of right thumb and excision of infraorbital lesion; x-ray therapy of hyperkeratoses of hands	Duration prior to treatment: not known; no recurrence of infraorbital lesion after 2 years, or thumb lesion after 5 months
5. B. H. 70 F	Received Fowler's solution intermittently from the age of 18 to 50 years as treatment for psoriasis	1. Large basal-squamous carcinoma of the scalp measuring 12 by 16 by 1 cm. at the site of previous psoriatic lesions 2. Basal-cell carcinoma of left supraorbital area	Multiple small hyperkeratoses of trunk. Patchy brownish gray hyperpigmentation of skin of trunk (developed shortly after onset of arsenic therapy)	Epithelioma—"about 44 years"	Wide local excision of scalp epithelioma including entire thickness of the scalp followed by primary skin graft; local excision of left supraorbital lesion	Duration prior to treatment: epithelioma—about 6 to 8 years; no recurrence or metastases 1.5 years after treatment
6. M. F.* 50 M	Received Fowler's solution, 20 minims or more daily, for 13 years starting at the age of 22 years as treatment for psoriasis	Multiple superficial epitheliomatosis, lesions scattered over chest, abdomen, back, upper and lower extremities	Multiple small punctate hyperkeratoses of palms and soles	Palmar and plantar keratoses—10 years; epitheliomas—16 years	Electrodesiccation of all epitheliomas and largest keratoses	New superficial epitheliomas treated at intervals for the past 12 years; no metastases
7. A. M. 52 F	Received Fowler's solution regularly for 3 months at age of 22 years for "rheumatism and chorea"	Basal-cell carcinoma of right infraorbital area	Patchy hyperpigmentation of neck, groin, and forearms; multiple keratoses of forearms and face	Epithelioma—27 years	X-ray therapy to epithelioma (4,500 r/a in 3 treatments)	Duration prior to treatment: epithelioma—1 year; no recurrence after 18 months
8. M. M. 69 F	Received Fowler's solution, 9 to 15 drops per day, for "about 1 month" as treatment for dermatitis at age of 42 years	Squamous-cell carcinoma of left 4th finger (1.5 by 5 by .5 cm.)	Multiple pigmented hyperkeratoses of forearms	Epithelioma—"about 25 years"	Wide local excision of finger epithelioma and radical left axilary lymph node dissection (nodes negative for metastases)	No recurrence or metastases 1.5 years after treatment
9. W. P. 59 M	Received Fowler's solution regularly for 9 months at age of 24 years as treatment for bronchial asthma	Basal-cell carcinoma of right ear lobe	None	"About 25 years"	Local excision of lesion including right ear lobe	Duration of epithelioma prior to treatment: about 4 years; no recurrence 1.5 years after treatment.

*Patient at Fort Snelling Veterans Administration Hospital.

exhibiting both keratoses and epitheliomas the average age at onset is 32 years for the arsenical keratoses and 51 years for the epitheliomas. This is in accord with previous observations that the age of onset of arsenical malignancy is earlier than that of usual skin cancers. According to Montgomery[13] the average age at appearance of precancerous keratoses is 44 years. The average age at the time of first exposure for the entire series is 27 years. The interval between the time of first exposure and appearance of the arsenical keratoses ranged from 1 to 26 years. The latent period between first exposure and onset of first epithelioma averaged nearly 28 years with a range from 16 to 44 years. A previous report by Hueper[9] indicates a range from 2 to 60 years in tabulating 13 cases of medicinal arsenical cancers. Montgomery's series showed a latent period from ingestion of arsenic to onset of keratoses from 1 month to 30 years.[13]

The amount and duration of arsenical medication appears to bear no regular relationship to the occurrence of the disease. Arsenical cancer may follow upon a rather brief medicinal exposure as in Case 8, where the duration of therapy was only one month. Peculiarly, there are instances of protracted arsenic ingestion failing to manifest any of the symptoms of either acute or chronic arsenism and exhibiting no dermatological lesions. This suggests the presence of some type of idiosyncrasy or sensitiveness existing to the element. In the 8 cases, excluding Case 6 (multiple superficial epitheliomatosis), there were 4 patients with more than 1 arsenical epithelioma. A total of 15 skin cancers occurred in these 8 cases. Six of these lesions were located on the head, neck, or face; 5 on the fingers or hand, and 4 occurred in the ankle region. Seven out of the 8 extremity epitheliomas occurred in the 5 patients exhibiting palmar and plantar keratoses, and all of these lesions on the extremities were of the squamous-cell type. However, as previously emphasized by Franseen and Taylor,[6] arsenical carcinomas are not invariably of the squamous-cell type. Among the 15 primary carcinomas in this series, 4 have been classified as basal-cell epithelioma, 10 as squamous-cell epithelioma, and 1 as mixed basal-squamous epithelioma.* All of the lesions in Case 6 were classified as the basal-cell epithelioma of so-called benign superficial epitheliomatosis. Radical regional lymph node dissections were carried out in 3 of the cases of epidermoid carcinomas of an extremity. Histological examination failed to reveal the presence of lymph node metastases in any of these specimens. Bland-Sutton[5] has stated that carcinomas of arsenical origin do not metastasize to the regional lymph nodes; however, Franseen and Taylor[6] report the presence of regional metastases in 7 patients.

Associated carcinoma of the internal organs occurring in patients with arsenical cancers have been reported infrequently.[6] The fact that one of Hutchinson's original cases had a carcinoma of the left lung at autopsy has been noted with interest. However, the coexistence of carcinoma of the lung in the Schneeberg miners formerly thought to be due to arsenic has been established as secondary to radioactive air of the mines rather than arsenic in mine ore. No instance of associated carcinoma of the internal organs has occurred in our series to date.

*Histological sections reviewed and classified by Dr. James S. McCartney.

Chemical and Histochemical Methods of Diagnosis.—Quantitative chemical and histochemical determinations of arsenic in the lesions, normal skin, urine, hair, and nails have led several investigators[13, 14, 17] to suggest that arsenical epitheliomas and keratoses are associated with a local concentration of arsenic in the tissues. Montgomery and Waisman,[14] using Osborne's histochemical method[17] and the Osterberg modification of the Gutzeit method[20] for the quantitative determination of minute quantities of arsenic in skin, concluded that cases of arsenical keratoses and epitheliomas are associated with increased local concentrations of arsenic in the lesions and urine. However, they reported instances in which the normal skin contained more arsenic than the lesions and some typical cases in which the amount of arsenic contained was too small to be detected by the quantitative chemical methods. Whereas the Osborne technique was positive for arsenic in all cases of arsenical epithelioma studied, cases of various other types of dermatosis without evidence of arsenic etiology have also shown positive results. The literature contains several reports of patients with classical arsenical keratoses known to be taking arsenic, in whom both the histochemical and chemical determinations are negative. To further confuse the issue it is known that arsenic may be present normally in the urine to the extent of 1 mg. per liter, depending on the environment of the patient, his occupation, and the type of food ingested. According to Billeter and Marfurt,[4] amounts up to 0.0097 mg. per 100 Gm. may occur normally in the hair and skin. Although the lesions of multiple superficial epitheliomatosis are thought by several investigators[1, 3, 17, 19] to develop as a direct result of long-continued arsenic medication, the laboratory data are noncontributory. Osborne, in a histochemical study of more than 20 sections from patients with this disease, found no correlation between the amount of arsenic seen in the sections and the presence of epithelioma. "Also as much arsenic was found in the normal skin away from the epitheliomas as in the skin immediately surrounding the lesion. Very little or no arsenic was found in the epithelioma itself."[19]

Studies by Watson and Larson[27] reporting an increased excretion of urinary coproporphyrin in patients receiving heavy metals or certain arsenic compounds, suggested to us the determination of urinary coproporphyrin excretion as a possible diagnostic procedure for cases of arsenical malignancy. Urinary coproporphyrin determinations* were carried out in 7 of the 9 cases

TABLE II. URINARY COPROPORPHYRIN DETERMINATIONS

CASE	URINE COPROPORPHYRIN GAMMAS PER DAY
1. P. R.	78
2. F. P.	143
5. B. H.	180
6. M. F.	142
7. A. M.	252
8. M. M.	107
9. W. P.	100

*An Improved Method for the Determination of Urine Coproporphyrin and an Evaluation of Factors Influencing the Analysis, Schwartz, S., Zieve, L., and Watson, C. J.: J. Lab. & Clin. Med. 37: 843, 1951.

Acknowledgment is made to Miss V. E. Hawkinson for the coproporphyrin determinations carried out in this study.

reported (Table II). The urinary coproporphyrin excretion was found to be within normal range in all cases of arsenical malignancy studied. B.A.L. (British Anti-Lewisite), 2.5 mg. per kilogram of body weight in equally divided doses was administered in Case 2 every 4 hours for 2 days and then twice daily for 5 days. Concomitant daily urinary coproporphyrin determinations failed to exhibit significant change.

Treatment of Keratoses.—We believe that arsenical keratoses must be considered potentially malignant lesions warranting active treatment. The keratoses may be controlled successfully either by surgical excision or by destruction by electrocautery. Surgical excision has the advantage of removing the entire lesion for microscopic study, and we consider it the treatment of choice for all suspicious lesions exhibiting recent change in size or growth rate, or having surface ulceration. However, cases with widespread multiple keratoses in close proximity are more practically controlled by electrocautery. This implies the necessity of punch biopsies of the suspicious lesions prior to treatment. More than one treatment is often necessary for complete eradication by this method. New lesions and recurrent keratoses are not uncommon and require similar management. Certainly, having recognized the premalignant nature of these lesions, one must never dismiss these patients, and must insist on careful follow-up examinations at regular intervals. Under such a regimen early malignant lesions can be recognized and destroyed by relatively simple means.

Treatment of Epitheliomas.—Carcinomas of the skin have the best prognosis of all malignant tumors and undoubtedly the prognosis is better in cases of arsenical epithelioma than with the usual type of skin cancer. This is particularly true of extremity lesions. The rate of local growth and invasion appears to be slower, and metastases occur less frequently and later in the course of the disease. However, these relative advantages do not ensure a favorable outcome. Inadequate or late treatment will lead to incurability and the ultimate death of the patient.

Treatment of Primary Lesions.—We believe that the treatment of the primary lesions of arsenical epithelioma should not differ from the management of the usual case of skin cancer, which in this clinic can be reduced to a choice of surgical excision or roentgen therapy. The choice of therapy will depend upon the location and extent of the lesions. Surgical therapy is preferable for lesions of the extremities and too often is used only after failure of irradiation therapy to control the disease. The surgical attack in any instance should be planned to insure adequate removal of the lesion with an ample margin of normal tissue. In advanced cases involving the skin of the extremities some type of amputation is usually necessary. Because of somewhat better cosmetic results, roentgen therapy is indicated for small, early cases occurring about the nose, eyes, or ears, where control of the lesion can be accomplished either by surgery or radiotherapy.

Treatment of Metastases.—Radical dissection of regional lymph nodes—cervical, axillary, inguinal, or iliac—is advisable in the treatment of metastatic squamous-cell carcinoma at these sites. Dissections should be done in con-

tinuity with removal of the primary lesion when possible. In other instances dissections are deferred until the primary lesions are controlled. Prophylactic lymph node dissections have become a routine practice in the management of advanced squamous-cell carcinoma of an extremity. In 3 cases of arsenical epitheliomas of the extremity in this series dissections were carried out in the absence of palpable lymph nodes. Microscopic examination of all nodes was negative in each case. It may be wiser in cases of arsencial epithelioma to defer regional lymph node dissection until the nodes become palpable and clinically suspicious. This approach may be particularly advantageous in those cases where, although the primary carcinoma has been controlled, one suspects that in time additional new carcinomas may arise from the keratotic skin. Under such circumstances the protective barrier of the regional lymph nodes may be worth preserving until there is reasonable evidence that they contain metastases.

SUMMARY

1. Nine new cases of arsenical epitheliomas of medicinal origin are reported.

2. It is significant that 8 of these cases were encountered during a two-year period among 110 new cases of skin cancer.

3. Diagnostic methods, including chemical, histochemical, and urinary coproporphyrin studies, are discussed.

4. Methods of treatment are presented.

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AN EXPERIMENTAL STUDY OF THE THROMBOGENIC PROPERTIES OF MAGNESIUM AND MAGNESIUM-ALUMINUM WIRE IN THE DOG'S AORTA

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IN 1864 Moore of London[1, 2] advocated the introduction of iron wire into aortic aneurysms. In 1879 Cowadi[1, 2] suggested the passage of an electric current through silver wire in an attempt to produce increased intrasaccular thrombosis. Since that time, sporadic reports of wiring, with or without electrolysis have appeared in the literature[3-8] culminating in the work of Blakemore and King. In 1938 these authors reported on their electrothermic method, using insulated coin silver wire for the deposition of clot on wire inserted into an aneurysm.[9] This technique enabled the authors to determine the rate of blood flow through the aneurysm as well as the amount of wire required to inactivate the aneurysm. In spite of Blakemore's successful application of this method during the past thirteen years in a large number of patients with a wide variety of thoracic and abdominal aneurysms,[10-12] mastery of his technique has been difficult for other surgeons to attain. In recent years the use of stainless steel wire, introduced into the sac without passage of electric current, has been advocated and practiced. The results of this procedure have not been overly encouraging in general use. For this reason, a metal of greater thrombogenic potential would be of value, and magnesium (and an aluminum alloy of magnesium) were studied in dogs' aortas.

We have been unable to find in the American literature during the past thirty years any reference to the use of magnesium wire in the management of aneurysms. However, Dörfler[13] philosophized on the possible value of magnesium wire as an agent to favor intrasaccular clotting and also pointed out that pure magnesium wire was brittle and difficult to handle. He added that magnesium alloyed with aluminum was pliable and workable, and hence would probably be of some value. It seemed worth while, therefore, to follow the lead of the German workers in this field and critically evaluate experimentally the thrombogenic properties of magnesium wire and an aluminum alloy of magnesium wire.

METHOD

Healthy adult mongrel dogs were used, and all operations were performed under aseptic precautions. The terminal abdominal aorta was exposed and mobilized through a left rectus muscle-splitting incision. After division of

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the deep circumflex iliac arteries, small paired dorsal vessels, and in some instances the inferior mesenteric artery, a 3 to 4 cm. segment of aorta was isolated between rubber-shod clamps. A longitudinal incision, 1 to 2 cm. in length was made on the anterior surface of the vessel and the wire introduced in the form of a double coil. In all animals the aortotomy was done at least 2 cm. above the trifurcation so that following closure of the vessel and removal of the clamps the wire would be displaced caudally and not be in contact with the suture line. The lumen of the aorta was washed frequently with isotonic saline solution during this interval. Following introduction of the wire coil, the aortic incision was closed with a continuous everting mattress suture of 00000 silk on an atraumatic needle (Deknatel). The abdomen was closed in layers and the animals given procaine penicillin for the first 48 hours postoperatively. Femoral pulses were palpable in all animals at the conclusion of the operative procedure.

RESULTS

Thirty animals were studied, using stainless steel wire (20 gauge), commercially pure magnesium wire (.025 inch in diameter), and an alloyed magnesium consisting of 98 per cent magnesium and 2 per cent aluminum wire (0.03 inch in diameter). The different types of wire were approximately equal in caliber. The alloyed wire was especially prepared after it was found that the magnesium wire, although possessing a high thrombogenic potential, was extremely brittle and therefore of dubious clinical value. The animals were sacrificed at 10 and 21 day intervals and the degree of thrombosis determined (Table I). Thrombosis was graded on a 0 to 4 plus scale as described in the Table I footnote. One animal exhibiting massive thrombosis which completely occluded the aortic lumen was discarded from the study, for it was felt that the thrombosis may have resulted from faulty suture technique in the aortic closure. All other animals had thrombus attached only to the wire, and no evidence of thrombus formation at the line of suture.

Necropsy Findings.—The findings at necropsy were:

Steel wire: Five animals were sacrificed 10 days, and 5 animals sacrificed 21 days, after introduction of No. 20 stainless steel wire into the aorta. In the 10 day group, thrombus formation on and about the wire did not exceed 2 plus, while there was 1 animal in the 21 day group exhibiting 3 plus thrombosis. The average thrombosis in both groups was 1.2. The steel wire did not become adherent to the aortic intima in any of these animals. The 21 day thrombi were firmer and whiter than the 10 day thrombi as might be expected with increased organization.

Magnesium wire: A similar number of animals were sacrificed at the same intervals following the introduction of magnesium wire into the abdominal aorta. The average thrombosis in the 10 and 21 day groups in this series was 2.6 and 2.4 respectively. Grossly, the thrombi were similar in all respects to those adherent to the steel wire. A significant difference in the 21 day find-

ings was the firm attachment of the wire to the aortic intima. In some areas the wire appeared to be enveloped by a grayish pseudomembrane which extended from the intima to the adjacent portion of the wire. No tendency to dissolution or change in the physical properties of the wire was noted at 21 days.

TABLE I

DOG	TYPE OF WIRE	DURATION OF EXPERIMENT (DAYS)	DEGREE OF THROMBOSIS*	ATTACHMENT OF WIRE TO INTIMA	DISSOLUTION OF WIRE
8	Steel	10	1	No	No
11	Steel	10	2	No	No
12	Steel	10	1	No	No
13	Steel	10	2	No	No
19	Steel	10	0	No	No
			Average 1.2		
24	Steel	21	3	No	No
25	Steel	21	1	No	No
26	Steel	21	1	No	No
28	Steel	21	1	No	No
30	Steel	21	0	No	No
			Average 1.2		
5	Magnesium	10	4	No	No
9	Magnesium	10	2	No	No
10	Magnesium	10	4	No	No
14	Magnesium	10	2	No	No
18	Magnesium	10	1	No	No
			Average 2.6		
17	Magnesium	21	2	Yes	No
20	Magnesium	21	2	Yes	No
21	Magnesium	21	4	Yes	No
27	Magnesium	21	2	Yes	No
29	Magnesium	21	2	Yes	No
			Average 2.4		
32	Mg.-Al. Alloy†	10	4	No	No
33	Mg.-Al. Alloy†	10	4	No	No
34	Mg.-Al. Alloy†	10	4	No	No
35	Mg.-Al. Alloy†	10	2	No	No
36	Mg.-Al. Alloy†	10	2	No	No
			Average 3.2		
37	Mg.-Al. Alloy†	21	3	Yes	Almost complete
38	Mg.-Al. Alloy†	21	3	Yes	Almost complete
39	Mg.-Al. Alloy†	21	4	Yes	Almost complete
40	Mg.-Al. Alloy†	21	4	Yes	Almost complete
41	Mg.-Al. Alloy†	21	3	Yes	Almost complete
			Average 3.4		

*Classification of Thrombi:

1—Thrombus between adjacent turns of wire at one or more sites.

2—Thrombus between adjacent turns of wire and extending for less than one-half the distance across circle formed by wire.

3—Thrombus between adjacent turns of wire and extending for more than one-half the distance across circle formed by wire.

4—Thrombus extending completely across circle formed by wire and partially or completely covering wire turns.

†Magnesium-aluminum wire containing 98 per cent magnesium and 2 per cent aluminum.

Alloyed magnesium wire: Because of the extreme friability of the magnesium wire, a more manageable type of magnesium wire was prepared. The addition of a small amount of aluminum made it possible to bend and twist the wire without breaking it. This wire was placed in the aorta of 10 dogs and the animals sacrificed at 10 and 21 days in an attempt to determine if modification

of the physical properties had influenced the thrombogenic properties of the magnesium wire. The average thrombosis in the 10 and 21 day groups was 3.2 and 3.4 respectively, and as far as can be determined in this series, the irritative properties of the metal had been enhanced by the modification. There was no intimal attachment or change in the physical property of the wire 10 days after its introduction. However, at 21 days, the wire had undergone almost complete dissolution and was identifiable as metallic particles enmeshed in the thrombus. Thrombus and metal were firmly attached to the intima at this time. (Fig. 1, *A* to *F*.)

Microscopic sections were made of representative specimens in the various groups. The intima, internal elastic membrane and media were intact in those aortas containing steel wire (10 and 21 days after insertion), magnesium wire (10 days after insertion), and the alloyed magnesium preparation (10 days after insertion). There was adventitial reaction coincidental to the aortotomy. This consisted of fibroplasia, area of ecchymosis, and lymphadenosis in scattered small periaortic lymph nodes. However, 21 days after insertion of the magnesium wire and the alloyed magnesium wire into the aorta, microscopic changes were evident. The grayish pseudomembrane attaching wire to intima consisted of finger-like processes of collagenous fibrous tissue extending from the inner aspect of the aorta into the lumen. At these sites the internal elastic membrane and intima were absent.

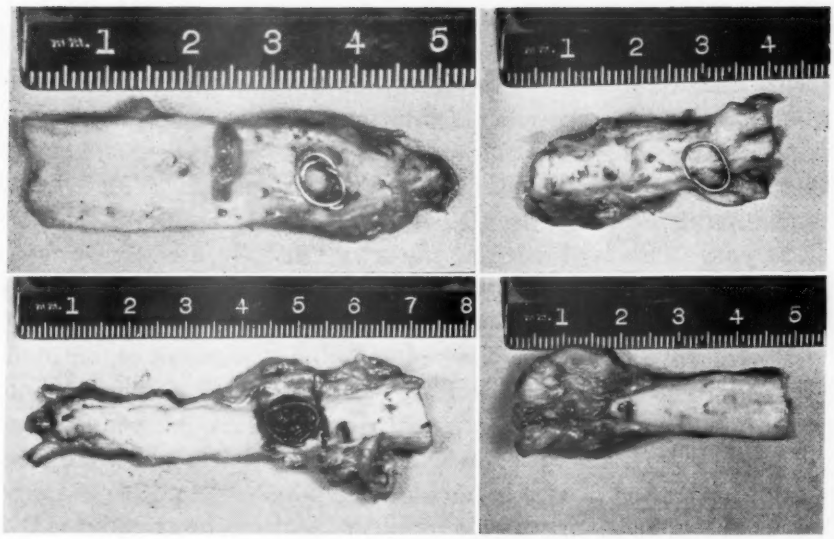
DISCUSSION

The study reported here suggests that magnesium, and particularly the alloyed aluminum derivative, is a more suitable material for the intraluminal wiring of saccular aortic aneurysms than the commonly used steel wire. Experimentally, the thrombogenic properties of the magnesium metal are twice as great as steel and of the alloyed magnesium preparation almost 3 times as great as steel (Fig. 2). An additional advantage of the magnesium wire is its eventual tendency to adhere to the intima, thereby minimizing the danger of its dislodgment from an aneurysmal sac with entry into the aortic stream. Conceivably this latter circumstance could give rise to obstruction and thrombosis of the aorta either at the level of the aneurysm, at the aortic bifurcation, or within the iliac vessels. It has been reported that the metal magnesium, when placed in the tissues, is eventually absorbed. Absorption might also be expected to occur in the aorta, and 21 days following the introduction of the magnesium-aluminum wire the metal appeared to be undergoing dissolution. The limited duration of the present study did not afford observations regarding the ultimate fate of the substance, however. Absorption would be an additional desirable factor minimizing the possible complication of subsequent erosion and rupture of the aneurysmal sac.

The magnesium wire and the alloyed magnesium wire cannot be visualized by x-ray after introduction into the aorta. When placed on x-ray film, their radiopacity is minimal.

Sterilization of the magnesium and alloyed magnesium wire was accomplished by immersion in 70 per cent alcohol for 20 minutes prior to its use.

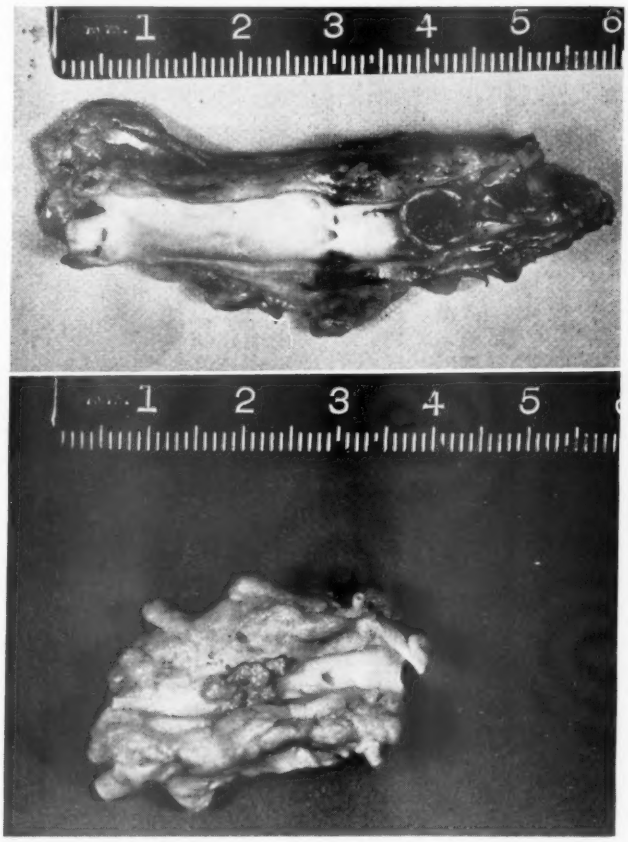
A. *B.*



C. *D.*

Fig. 1, *A-D.*—*A*, Dog 13. Steel wire in aorta for 10 days, showing the wire with a 2 plus thrombus approximately 1 cm. above trifurcation. *B*, Dog 25. Steel wire in the aorta for 21 days, showing wire at the trifurcation with a 1 plus thrombus. Suture line with no attached thrombus is visible. *C*, Dog 10. Magnesium wire in the aorta for 10 days, showing wire with adherent 4 plus thrombus. *D*, Dog 21. Magnesium wire in the aorta for 21 days showing wire above trifurcation with extensive intimal fixation and 4 plus thrombus.

E.



F.

Fig. 1, *E* and *F.*—*E*, Dog 34. Alloyed magnesium-aluminum wire in the aorta for 10 days, showing wire at the trifurcation with attached 4 plus thrombus. The upper portion of the suture line is visible and shows no evidence of thrombosis. There was no attachment of the wire or the thrombus to the lower portion of the suture line. *F*, Dog 40. Alloyed magnesium-aluminum wire in the aorta for 21 days, showing 4 plus thrombus above the trifurcation. Particles of the wire were enmeshed in the thrombus, which is firmly adherent to the intima.

Cold sterilization was preferred to obviate changes in the metal coincidental to boiling. Mr. R. T. Wood's recommendations for the clinical use of the magnesium-aluminum alloy were as follows:

"With regard to the sterilizing of the magnesium alloy wire, I would recommend boiling in water for 10 minutes as the safest of the three methods available to you. This will discolor the wire but should cause no measureable increase in diameter and it will not affect the structure of the alloy. There are certain precautions that should be taken, however. If the sterilizer is metal, the wire should not be allowed to touch the sides or bottom. If the wire is suspended by a hook while in the boiling water, the hook should be of glass or rubber coated. The best practice would be to suspend the coil to be sterilized with an extra loop of magnesium alloy wire. If these precautions are taken and the wire does not come out of the sterilizer clean and free from corrosion product, distilled water should be used in the sterilizer."

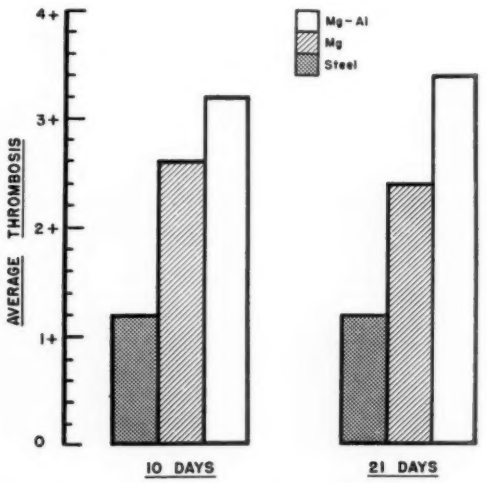


Fig. 2.—Shows the average degree of thrombosis in each group of animals in which the steel wire, the magnesium wire, and the alloyed magnesium-aluminum wire were used. The scale of 0 to 4 plus has been described in Table I. There were 5 animals in each group at 10 days and also at 21 days.

The alloyed magnesium wire is malleable and its introduction into an aortic aneurysm could be readily accomplished by means of the needle, with removable stylet, which is now utilized for the insertion of stainless steel wire. In view of the marked thrombogenic property of the alloyed magnesium wire, it is our present belief that the use of this wire should be restricted to saccular aneurysms of the thoracic and abdominal aorta. Were it to be employed in fusiform aneurysms, the danger of rapid thrombus formation and possible embolization would exist. Although this objection is purely theoretical, we plan to limit the initial use of alloyed magnesium wire to cases of saccular aneurysms of the aorta.

SUMMARY

The thrombogenic properties of three metals (stainless steel, magnesium, and an alloy of aluminum-magnesium) were tested in the aorta of 30 dogs. It

was found that magnesium wire is approximately twice as irritative as stainless steel wire with respect to thrombus formation following its insertion into the abdominal aorta. The alloyed magnesium wire, especially treated to make it less brittle, exhibited a further increase in thrombogenic potential. The clinical application of these findings in the treatment of aortic aneurysms is discussed briefly.

CONCLUSIONS

1. Magnesium wire is approximately twice as thrombogenic as stainless steel wire when placed in the abdominal aorta of dogs.

2. A less brittle alloy of magnesium wire containing 2 per cent aluminum has a greater thrombogenic potential than the untreated magnesium wire, and would probably be satisfactory for clinical use.

3. The physical properties of the magnesium wire and of the alloyed magnesium wire are presented.

4. The use of alloyed magnesium wire in the treatment of saccular aortic aneurysms is discussed.

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MICROSCOPIC OBSERVATIONS OF THE LIVING MAMMALIAN KIDNEY: THE EFFECT OF CRUSH INJURIES, SHOCK, AND ADRENALIN ON THE CORTICAL BLOOD FLOW

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THE term "crush syndrome" was originally used to describe a clinical condition characterized by oliguria following crushing injuries in air raid casualties.[1] The injury produced a state of shock which responded to transfusion with the return of normal blood pressure. After recovery from shock these patients developed oliguria and uremia, and usually died in about a week from kidney failure. In the last ten years a similar clinical course has been described in a variety of other conditions such as burns, severe noncrushing injuries, and obstetrical complications. All these clinical states, including the "crush syndrome," appear to produce similar pathologic changes in the kidney which Lucke[2] has called lower nephron nephrosis.

A great deal of experimental work upon animals has been done in an attempt to throw light upon the etiology of these kidney changes. Much of this work has entailed observations of kidney function immediately following injury during the period of posttraumatic or hypotensive anuria. *Posttraumatic anuria* should be carefully differentiated from the *crush syndrome* because the renal phenomena observed in this early period are not necessarily present in the later stages of the true crush syndrome. The experimental observations of posttraumatic anuria are usually made in the presence of shock, whereas the anuria of the crush syndrome follows a latent period, which includes the period of shock, and exists for several days in the presence of a normal or elevated blood pressure. Anuria of long duration following injury in animals has only been produced by the simultaneous administration of blood or muscle pigment.

There is thus some confusion in the literature regarding terminology. Experimental observations designed to throw light on the crush syndrome have sometimes been made on animals with posttraumatic anuria. There are several theories, however, that have arisen out of a great deal of very good experimental and pathologic work, as to the cause of the crush syndrome. These may be included under the following headings: 1. Blockage of renal tubules by various pigments such as myoglobin and methemoglobin[2-4]; 2. renal anoxia resulting from the ischemia of shock[5]; 3. tubular damage by some unknown toxic agent released from the crushed tissues[4, 6]; 4. renal vascular disturbances, such as short circuits and arterial spasm.[2, 4, 7, 8]

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During our past studies of the microscopic vascular bed in about 400 animals and 100 human beings[9, 10] we have consistently observed that following severe trauma many of the small peripheral vessels, in all parts of the body studied, show embolic occlusion by circulating clumps of red blood cells, especially in the presence of vasospasm. This produces a widespread vascular "stasis" (blockage) of the terminal vessels throughout the body and remote from the area of trauma. Under such circumstances arteriovenous shunts are often seen to open up and short-circuit the blocked vessel, and thus maintain the circulation.

In view of this, it seemed reasonable to assume that a similar phenomena would occur in the cortex of the kidney if the red cell clumps were large enough and the vasospasm sufficient to produce obstruction. The branches of the interlobular arteries might very easily be occluded in this manner rendering the entire cortex ischemic, and this could be an important factor in the production of renal failure in the crush syndrome.

The vascular stasis thus produced might be responsible for the local tubular anoxia and damage, and this obstruction to blood flow through the cortex might cause "short circuits"[7] or "sponges"[11] to open up. Spasm of large vessels which is known to exist in cases of crush syndrome might extend into the peripheral vascular tree and enhance the degree of obstruction.

In order to investigate this theory we produced crushing injuries in animals, followed renal function tests, and observed the amount of intravascular agglutination of red blood cells from day to day in the easily accessible conjunctival vessels. Then at various intervals we exposed a kidney and observed blood flow in the cortical vessels. As our observations will show, we were able to produce a mild crush syndrome but we could not reproduce the true syndrome with fatal anuria. Consequently the experiment was extended to include observations of renal cortical blood flow not only in these crushing injuries but in other forms of trauma, in hemorrhage, and in the presence of vasospasm induced by adrenalin. Blood pressure records were made in each experiment as an aid to the interpretation of observations made of the peripheral blood flow.[10]

METHODS

Crushing Injury.—We attempted to produce the "crush kidney" syndrome in rabbits by binding both legs tightly from toes to hips with a wide elastic tourniquet, and then hammering both legs with a rubber mallet; the tourniquet remained in place for four hours. The degree of trauma was just mild enough to permit most of these animals to survive the period of acute shock without supportive blood transfusions. These rabbits were kept in metabolism cages from one week prior to the crush until death. They were fed water, rabbit chow, and lettuce, ad libitum. The urine output per twenty-four hours was measured for volume, and routine urinalysis was done daily.

Urea Clearance Tests.—Urea clearance tests were done every second day, as follows: The bladder was emptied by catheter, a blood sample removed from the

ear vein two hours later and the bladder again emptied in another two hours. Blood and urea nitrogen determinations were done by the method of Van Slyke and Cullen.[12] Maximum urea clearance was determined because rabbits do not have an augmentation limit.[13] This was then calculated on the basis of surface area and expressed as cubic centimeters per square meter per hour. Surface area was calculated from the rabbit's weight using Meek's[14] formula: S.A. = $k \sqrt[3]{W^2}$, where the constant k for rabbits (excluding ears) is 0.108.[15]

Tourniquet Experiments.—In other rabbits, we applied a wire tourniquet, enclosed in thin rubber tubing, to the left thigh, tightened it with pliers (after hooking it over the ischial tuberosity), until the femoral pulse was obliterated. This was the method used by Trueta.[7]

Burns.—Both legs were shaved and dipped in water at 100° C. for 6 seconds up to a previously determined level representing a 5 to 10 per cent surface area burn.

Hemorrhage.—Blood was removed from the carotid artery in 10 c.c. amounts until the blood pressure fell to 20 to 30 mm. Hg.

Adrenalin.—Adrenalin was given into an ear vein in amounts ranging from 0.01 mg. to 0.5 mg.

Arterial Blood Pressure.—Arterial blood pressure was measured by a mercury manometer connected to a cannula in the carotid artery.

Method of Observing Renal Cortical Blood Flow.—The great work of Richards and Walker,[16] involving microscopic observations of the living kidney was done on frogs, whose kidneys are thin enough to permit excellent transillumination. However, we had decided that our observations should be made on mammals, which are phylogenetically closer to the human being. Mammalian kidneys are far too thick to permit transillumination; and reflected lighting, such as used by Walker and Oliver,[17] failed to yield sufficient clarity for observations of the blood flow, and also limited the field of observation to the most superficial part of the renal cortex.

A 5 mm. fused quartz rod was drawn out into a fine curved tip, about 0.6 mm. in diameter at its end which was ground and finely polished. The rod, 15 inches long, conducted light from a 500-watt tungsten lamp separated from the rod by a water filter. The tip of this rod was gently inserted into the substance of the decapsulated kidney, which had been exposed by a posterolateral muscle-splitting incision in the rabbit, lightly anesthetized with intravenous Nembutal. The point of the quartz rod was carefully inserted until it was very near the surface of the kidney, avoiding any pressure outward on the illuminated tissue; the brightly illuminated field was 3 to 4 mm. in diameter. Mammalian Ringer's solution at 38° C. constantly bathed the kidney, and microscopic observations were made using water immersion lenses. The addition of a little blue dye to the water filter increased the contrast and clarity. Interfering respiratory movements were decreased by resting the kidney on a metal mould, mounted on a metal arm. Figs. 1 and 2 show the assembled apparatus. By this means, we were able to observe the tubules and blood vessels of the surface of the cortex, to a depth of about 100 μ. The clarity was such that the brush borders of the proximal tubules could be seen quite well.

Attempts were made to visualize deeper structures by shaving off thin sections of the kidney, as was done by Frey[18] but in every instance, hemorrhage obscured the field, and this could not be controlled. However, if the blood were washed away quickly by the Ringer's solution a clear picture of the deeper structures, including glomeruli could be obtained. This method was discarded because of the severe trauma involved. Magnifications ranged from ×50 to ×600. As long as the tissues were handled very gently, and kept warm and moist with Ringer's solution, the blood flow fulfilled the conditions of normality outlined in previous communications.[9, 10]

We were aware that vasomotor changes might be interfered with by the influence of anesthesia, and that handling the kidney might provoke abnormal renal vasomotor changes. We attempted to minimize these factors by using a minimum of anesthetic, and by avoiding unnecessary handling of the tissues.

Fig. 1.—Transillumination of kidney cortex. *A*, Light source; *B*, quartz rod; *C*, constant temperature bath; *D*, Ringer's solution overflow; *E*, kidney.

OBSERVATIONS

Fig. 3 shows some of the changes in renal function that occurred in ten rabbits that were subjected to crush injury of the legs as described. Although every rabbit developed some impairment of renal function for about five days, none developed a fatal anuria. Sections of the kidneys, one to two weeks after crush, showed a moderate degree of hyaline and droplet degeneration of the convoluted tubules, and many pigment casts; the liver showed some central lobular necrosis. These findings are suggestive of mild crush syndrome.

As far as we are aware, no person has produced a syndrome in animals similar to the crush syndrome seen in human beings.[19-21] Apart from acute experiments terminating in shock, we were unable to find reference to the experimental production of oliguria or anuria, lasting several days and terminating in uremia, by traumatic means alone. Several investigators have produced, as we did, some degree of impairment of renal function in animals that survived the period of acute shock.

Realizing, therefore, that we were unable to reproduce the human crush syndrome in animals, we decided to approach the problem indirectly. We observed the effect on renal cortical blood flow of various separate conditions which might contribute to the production of posttraumatic anuria.

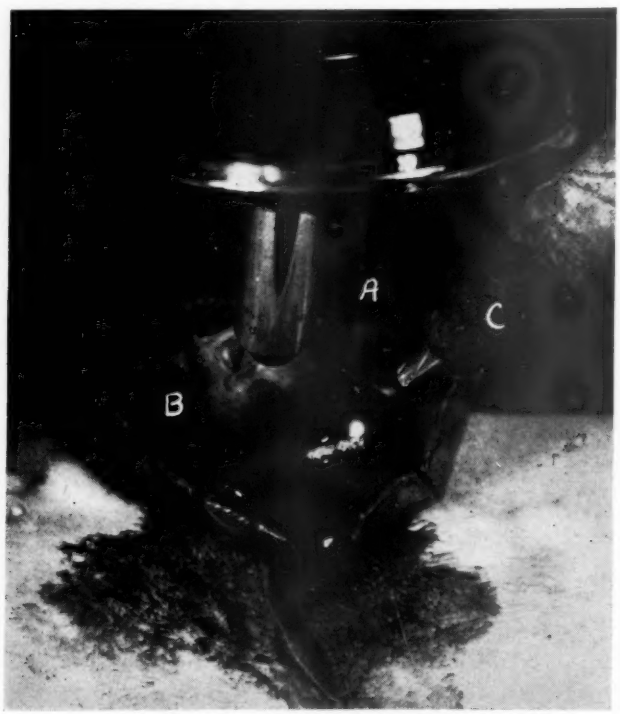

Fig. 2.—Close-up view showing an area of kidney cortex illuminated by the quartz rod tip. *A*, Quartz rod; *B*, metal support for kidney; *C*, Ringer's solution overflow.

We were concerned as to whether the fine-pointed quartz rod might in itself produce a local vascular reaction to injury. Once the technique was perfected, however, one could observe perfectly normal flow with no evidence of stasis, diapedesis of cells, or intravascular agglutination for as long as three hours.

The vessels visualized were the interlobular or radiate artery and vein, surrounded by intricate capillary networks. The venules leading to the interlobular vein were larger and more numerous than the arterioles. These vessels could also be differentiated by the direction of blood flow and presence of pulsations.

Under normal conditions blood flow was rapid and smooth, so that individual red cells could not be distinguished. There was no tendency on the part of thered cells to clump together or stick to the vessel walls. In the smallest capillaries, red cells moved rapidly and smoothly in single file. The larger vessels could be seen to change diameter under various influences. In all these respects, the renal cortical flow resembles blood flow elsewhere in the body. In addition, some intermittence of blood flow in the renal cortex is often seen, so that not all vessels are filled at once, but a few are empty. Reversal of direction of blood flow is also quite a common observation.

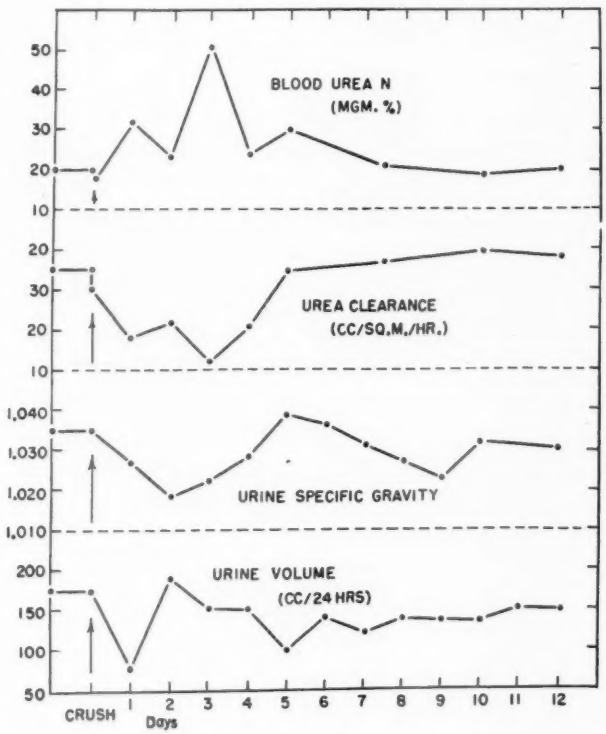

Fig. 3.—Changes in renal function following crushing injuries; average findings in ten rabbits.

Only a very few glomeruli were seen, as the microscopic field was so superficial. Blood flow through the capillary tuft is very rapid and resembles normal capillary blood flow elsewhere in the body. Occasionally a shunt between the afferent and efferent arteriole of a glomerulus can be seen, with static red blood cells within the glomerular capillary loops when the shunt is open.

The Effects of Various Forms of Trauma.—The effects of 3 forms of trauma (crush injuries, burns, and tourniquet experiments) were studied in 17 rabbits. The blood pressure was followed during each experiment while the kidney was being observed.

Crush injuries: Eight animals were studied in this group, and the kidneys observed at varying intervals after trauma.

We were surprised to find that immediately following crushing injury to the legs, and for several days afterward, blood flow through the cortex of the kidney was not completely stopped. The flow was definitely slower than normal, and there were frequent areas of stasis in capillaries, arterioles and venules; occasionally a static interlobular vein could be seen. There appeared to be vasoconstriction, especially during the first twenty-four to forty-eight hours following trauma. Agglutination of red cells was apparent, presenting in the 20 to 30 μ vessels as large clumps, or just as a granular type of flow. In the capillaries these clumps could be seen intermittently obstructing the lumen, and often causing a reversal of the direction of flow, or complete stasis.

The arterial blood pressure in these animals dropped to 70 to 80 mm. Hg for the first forty-eight hours following trauma and then returned to normal or as high as 130 to 140 mm. Hg.

Burns: Three animals were studied in this group.

The renal cortical blood flow following burns was much the same as that seen in crush injuries, except that the clumping was the most notable abnormality. Constriction of capillaries and arterioles was less predominant. Slowing of flow, intermittence and reversal of the direction of flow, and stasis, were all seen frequently. Slowing of flow was not as marked as in crush injuries.

Tourniquet: Six animals were studied in this group.

Following the removal of a wire tourniquet from the thigh, the animal gradually became lethargic and the blood pressure fell to about 70 to 80 mm. Hg. The renal cortical blood flow appeared slower than normal, and there was a moderate amount of vasoconstriction. Stasis, although present, was not a predominant feature. After twenty-four hours, red cell clumping was more apparent in addition to these changes.

The Effect of Hemorrhage.—The most notable effect of low blood pressure is a generalized constriction of the arterioles and capillaries visualized in the renal cortex. Associated with this is a decrease in the rate of blood flow through these vessels. There is an increasing intermittence of flow, and as the blood pressure reaches 20 to 40 mm. Hg, stasis is observed quite frequently, and a vasodilatation occurs. Fairly rapid blood flow has been observed in some of these vessels in animals with a blood pressure as low as 20 mm. Hg. We have seen the same changes in the renal cortical vessels in animals after severe hemorrhagic shock and without anesthesia. This would suggest that the anesthetic had not significantly interfered with the renal vasomotor response observed.

Adrenalin.—The effect of adrenalin was studied in ten animals. The vascular response varied in degree in different rabbits.

The changes seen in the renal cortex appeared almost immediately. There was marked vasoconstriction, especially of the arterioles and capillaries, with associated slowing of blood flow and complete cessation of flow in many vessels. There appeared to be some dilatation of the larger interlobular venules. Some of the capillaries in which the blood flow had stopped were filled with static red cells and others were completely empty of blood. In a few capil-

laries there was intermittence of flow and occasional reversal in the direction of flow. These changes lasted as long as the adrenalin affected the arterial blood pressure. If very large doses of adrenalin were given (0.5 to 1.0 mg.) the entire microscopic field would blanch, with complete cessation of flow in all vessels. Many more capillaries would appear completely empty of red cells. It would be emphasized that the Nembutal anesthetic may have interfered with the normal vasomotor responses. The vasoconstriction was replaced by a marked vasodilatation and rapid blood flow as the effect of adrenalin wore off.

If adrenalin was given to an animal in which there was gross intravascular clumping of red cells (as seen in the posttraumatic group) the effect was more striking. Smaller doses of adrenalin produced immediate and complete stasis in all vessels under observation. The kidney cortex turned pale and this persisted until the blood pressure returned to normal, in 2 to 5 minutes.

DISCUSSION

The mechanism of cortical ischemia was studied because it is considered to be the primary factor in the pathogenesis of the renal failure in the crush syndrome.

We were unable to produce the true crush syndrome in rabbits and we were thus able to provide only indirect proof of our hypothesis that the renal failure is due to a blockage of the cortical vessels in the kidney by agglutinated clumps of cells in the presence of vasospasm. Only rabbits were studied, and we did not take recourse to the injection of blood and muscle pigments to aid in reproducing the clinical crush syndrome.

Besides observing crush injuries, we have studied what we considered to be the basic physiologic components of the crush syndrome, namely, intravascular agglutination, vasospasm, and shock, in relation to renal cortical blood flow.

The effect of *intravascular agglutination of red blood cells,* with and without shock, was studied in burns, crushing injuries, and tourniquet shock. Varying degrees of stasis were produced.

The effect of *shock* in the absence of intravascular agglutination was observed in hemorrhage where no stasis was seen.

Vasospasm in the absence of red clumps or shock was illustrated by the adrenalin experiments. Complete cessation of flow was produced by large doses.

It was concluded that cortical ischemia was more easily produced by a combination of two or all three of these factors. Vasospasm (adrenalin) in the presence of intravascular agglutination, however, produced the most dramatic effect.

We do not know whether or not the phenomena observed in the outer 100 μ of the kidney cortex mirror what is happening at a greater depth. One would expect this to be a valid sample since the pathologic picture is usually similar throughout.

In this study we have duplicated some of Trueta's experiments in which, by injection technique, he demonstrated cortical ischemia soon after injury or in the stage of posttraumatic anuria. By direct observation, we found cortical flow persisting, contrary to his findings.

SUMMARY

1. An attempt has been made to clarify terminology and point out the difference between the clinical entity of crush syndrome and experimental posttraumatic anuria.

2. We have been unable to produce in rabbits the crush syndrome as seen in human beings. As yet, true crush syndrome has apparently never been produced in experimental animals, without supplementing the crush injury with some other factor such as injection of muscle pigments.

3. A technique has been described for observing cortical blood flow by transilluminating the kidney cortex of the rabbit. Tubules and small vessels including the finest capillaries with individual red blood cells can be observed by this method.

4. A modification of this technique, in which thin layers of cortex are removed, revealed deeper structures, and glomeruli were visualized.

5. The effect upon cortical blood flow of crush injury, tourniquet shock, adrenalin, and hemorrhage have been studied.

6. We were unable to confirm presently held views based on experiments using injection techniques, that complete cortical ischemia occurs in certain types of tourniquet shock in rabbits.

CONCLUSION

Evidence has been presented which suggests that clinical crush syndrome is due primarily to renal cortical ischemia produced by blockage of the interlobular artery or its branches by circulating clumps of red blood cells in the presence of vasospasm.

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OPEN SAFETY PIN IN STOMACH

Method of Removal

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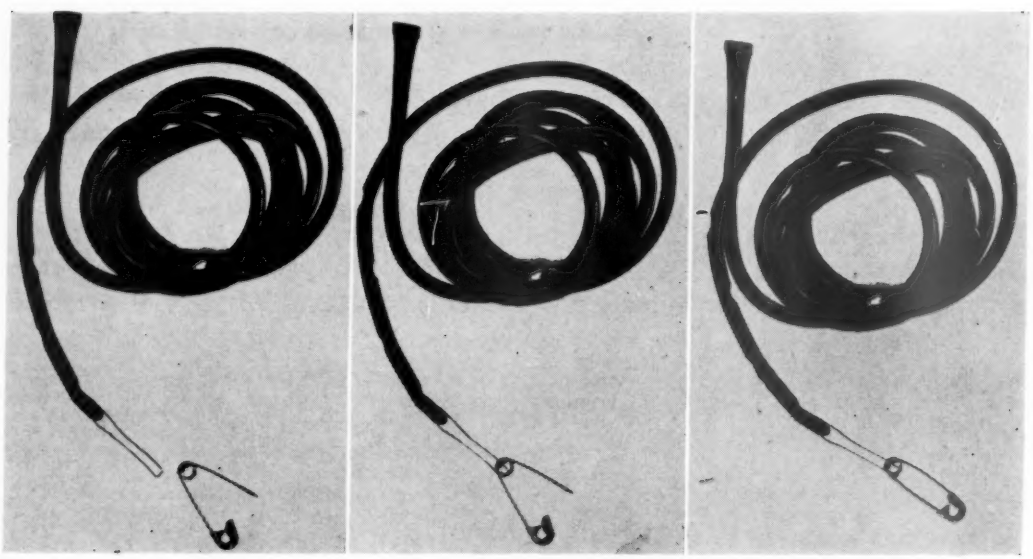
OPEN safety pins in the gastrointestinal tract may be treated conservatively and in 78 per cent of the cases can be expected to pass successfully.*

If surgical intervention for an open safety pin in the stomach is indicated, the accepted approach has been to perform a laparotomy, to close the pin by manipulation through the stomach wall without a gastrotomy, and to allow the closed pin to pass spontaneously.

An approach I have used successfully is suggested. A Levine tube is prepared with a small metallic loop through the tip end. This may be made of wire (Fig. 1) or a closed safety pin. The Levine tube is introduced through the mouth into the stomach. A small upper abdominal left paramedian incision is made. With no difficulty, the open safety pin and the Levine tube can be located by palpation through the stomach wall, and in young children can even be visualized through the thin wall. The metallic loop and the open safety pin can be engaged with ease and the pin closed. The tube, together with the pin, is then withdrawn.



A. *B.* *C.*

Fig. 1.—Levine tube with metallic loop through the tip. (*A*) Approaching the open safety pin. (*B*) Engaging the safety pin. (*C*) Safety pin closed and ready for removal.

This method has several advantages: (1) There is no contamination from the gastrointestinal tract. (2) The period of observation and roentgenologic follow-up is not required, for the pin is no longer a problem. (3) The patient may be discharged as early as twenty-four hours postoperatively.

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*Ladd and Gross: Abdominal Surgery in Infancy and Childhood, Philadelphia, 1948, W. B. Saunders Company.

Case Reports

A VITALLIUM REPLICA ARTHROPLASTY ON THE SHOULDER

A Case Report of Aseptic Necrosis of the Proximal End of the Humerus

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THE shoulder, as a rule, is not considered a suitable joint for possible arthroplasty by interposition of either absorbable or nonabsorbable material. However, it is felt that there is the occasional specific indication for nonabsorbable replica arthroplasty in the shoulder whenever the muscles and tendons are biologically sound, or relatively so.

Those cases which may be considered for the Vitallium replica arthroplasty are those in which the shoulder is solidly or partially ankylosed, as is occasionally seen following acute joint infection, certain fractures into the joint, certain osseous dislocation complications and the cases demonstrating abnormal tumerous osseous structure of the proximal end of the humerus. Included in this latter condition will be the benign tumors of bone and bone infarcts, where the articular surface has been encroached upon and disrupted, and the joint has become partially or solidly ankylosed, yet the rotator cuff and the shoulder muscles appear functionally in order.

Aseptic necrosis of the proximal end of the humerus occasionally occurs following dislocation of the humerus. It has been observed in caisson disease of the "sand-hog" and also demonstrated in aviators and submarine seamen suffering from the "bends." It is usually accompanied by severe osteocopic pain, restriction of scapulohumeral motion, and eventually ankylosis, while the rotator cuff and accessory muscles are relatively sound.

The following demonstrates a case of aseptic necrosis of the proximal end of the humerus, following traumatic dislocation, in a young, healthy man. The dislocation was complicated by degeneration of humerus head cartilage and incomplete fibrous ankylosis, chronically, severely painful, particularly in the proximal one-third of the humerus.

CASE REPORT

J. F. (USMH No. 219048), a 22-year-old, white, able-bodied seaman, entered the United States Marine Hospital, Staten Island, Dec. 10, 1950, with a painful, ankylosed left shoulder. He gave the following pertinent history: On Jan. 30, 1950, at sea, off the coast of Texas, he was tossed by a wave from the ship's bridge to the deck below, dislocating the shoulder in the fall. Before being rescued he had two more hard falls, jostling his useless arm and shoulder. Fourteen hours later he was taken to New Orleans, La., U. S. Marine Hospital. The shoulder was reduced, no fracture was found, and a Velpeau dressing was applied. He was discharged, to return in three weeks for removal of the

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bandage and a course of physiotherapy. However, he returned to his ship, which was en route to New York, and he reported to the U. S. Marine Hospital, Staten Island, on Feb. 10, 1950.

On admission, as the dressing was removed, the shoulder was found reduced; however, there was considerable nerve and vascular damage in the involved area. It was felt that he had a left brachial plexus injury involving chiefly the axillary, radial, medial, and antebracheal cutaneous nerves. He had a fairly large hematoma in the left upper arm, medial side, near the axilla, with considerable edema of the elbow, and palpable thrombi were noted in the basilic and cephalic veins on the left. He had a complete wristdrop. Roentgenograms again were reported as noncontributory (not remarkable). The routine gamut of treatment including abduction arm splint, cock-up wrist splint, and electrical stimulation, as well as routine physiotherapy was continued through April, 1950, when patient requested his discharge. He was discharged with a cock-up wrist splint with Bunnell's finger attachments.

The significant findings at time of discharge were: Fibrous ankylosis of the shoulder, considerable continuous deep bone pain even at rest which frequently awakened him at night, necessitating analgesics. There was normal range of elbow and wrist motion passively; however, radial nerve palsy was still present, and he had only a trace of triceps and deltoid function; sensation had returned to the skin of the shoulder and the cutaneous innervation of the arm. No roentgenograms were taken at the time of his discharge to outpatient status. For ten weeks he was then treated as an outpatient. June films in 1950 showed increased density of the proximal one-fourth of the humerus, including the head, with irregularity of the humerus joint surface. The shoulder was still painful and had a rubbery ankylosis. From June to October, 1950, he returned to sea. However, after his second trip he discovered that he could not continue, due to the arm and shoulder pain, particularly at night.

On Oct. 10, 1950, he returned to the hospital and the diagnosis of aseptic necrosis of the head of the humerus and proximal one-fourth of the shaft, as well as degenerative joint disease was established by direct biopsy and inspection of the joint. At exploration of the rotator cuff the cortical bone of the shaft of the humerus was found biologically relatively sound. The deltoid function had returned to good force, as had the triceps function, and most of the radial nerve involvement had regained function. There was moderate contracture of the adductors (latissimus dorsi, teres major, and some of the pectoralis). In view of this condition the indication appeared sound to use a nonabsorbable replica as part of an arthroplasty to establish some scapulohumeral motion with curettement for the relief of pain. The patient was continued on active physical medicine until the Vitallium replica* was prepared. An assortment of acrylic replicas were first designed, used in cadavers and studied for the best approach for each until a satisfactory one was decided upon (Fig. 1). On Dec. 12, 1950, an arthroplasty was done with a superior-posterior approach to the shoulder and the use of the Vitallium replica as described.

The patient had an uneventful postoperative course and the severe aching pain disappeared with surgery. At time of surgery and following, it was found that the latissimus dorsi, pectoralis, and teres major were so contracted that they permitted only 60 degrees abduction, flexion to 110 degrees, and extension to 30 degrees, with 30 degrees internal and no external rotation of the shoulder. The deep osteocopic pain present prior to surgery never returned. The patient was discharged Jan. 25, 1951, to help his father build a house. He was to continue weekly checkups and special exercises.

Up to the time of the last follow-up examination, April, 1951, this patient's shoulder had remained asymptomatic and without pain. He was able to do full carpenter work. By the first of May he had returned to sea. Examination of the operated shoulder showed definite improvement in range of motion, still improving. He had full adduction across chest as well as internal and external rotation. He had free abduction to 85 degrees and beyond this the scapula followed to full overhead motion. He had full posterior extension

*Prepared by Austinal Laboratories, New York.

of the arm. All motion was painless, there was no locking or clicking and he was exceedingly satisfied. There was still some deltoid weakness and wasting from the original injury.

Pathological examination of the tissue removed at operation revealed aseptic necrosis of the head of the femur.

Fig. 3 demonstrates the shoulder 70 days postoperatively, and further shows some range of motion by roentgenograms and photographs.

Fig. 1.—The Vitallium replica as originally constructed. The shank was shortened one and three-quarter inches in the case described here, as that was deemed long enough.

METHOD OF VITALLIUM REPLICA ARTHROPLASTY

Under intratracheal general anesthesia, the recumbent patient's trunk is put in a modified Fowler's position and a sandbag is placed under the shoulder which is to be operated on. Following operative preparation, a drape is arranged with the arm free. A saber incision is then made over the top of the shoulder, as described by Codman, at the level of the acromioclavicular joint. The acromion is then exposed, and by using a small osteotome, the deltoid muscle is released with periosteum and cortical bone in one piece. The acromion is

A. B.

C.

Fig. 2.—Pre- and postoperative roentgenograms of the left shoulder.

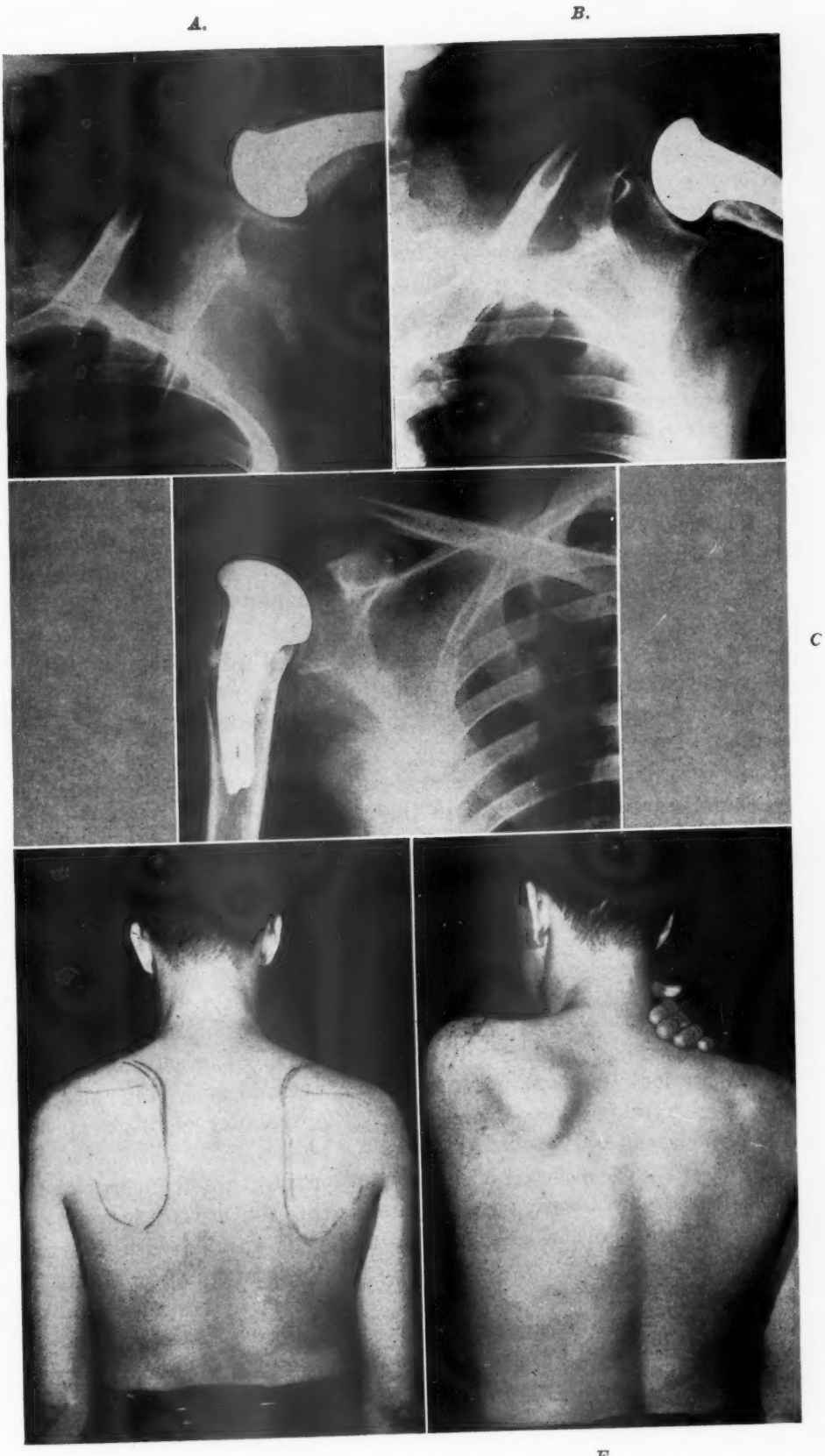

Fig. 3.—Roentgenograms and photographs 70 days postoperative, demonstrating assorted positions.

subtotally removed sparing the acromioclavicular joint and three-eighths inch of the acromion. The coracoacromial ligament is cut and a small section is removed. Care is taken not to cut the coracohumeral ligament, as it is felt that this is one of the primary ligaments preventing dislocations of the shoulder. This immediately gives greater range of motion of the scapulohumeral joint.

Electrocautery is preferred for hemostasis to expedite the procedure.

The greater tuberosity of the humerus is then identified, also the supra- and infraspinatus muscle insertions on the humerus. By blunt dissection the crease between the bellies of the supra and the infraspinatus muscles is separated down to the capsule from the insertion proximally at least two inches. The joint is then opened, as illustrated, and the articular part of the head of the humerus made accessible.

This approach was checked on several cadavers, as well as past experience reviewed, and it was found the best for accessibility to the articular cartilage and to the shaft for curettement, and because it makes possible the insertion of the replica without disturbing the cuff very much. Also, one must again note that the articular cartilage points upward and posteriorly in the neutral position.

Using gentle retraction for exposure, and small thin gouges, the whole head can be removed rapidly down to the capsule attachment, sparing all the cuff and other tendon attachments. This then gives free entrance to the proximal end of the humeral shaft.

In the case described here, the cortical bone below the cuff appeared grossly normal, however, the cystic areas in the cancellous portion extended down the shaft approximately three and one-half inches. This degenerated-appearing tissue was all curetted out.

Using the greater tuberosity proximally, and the epicondyles distally, for alignment the Vitallium replica is placed firmly into its proper position, facing upward and posteriorly. The head of the replica is so designed (oblong egg-shaped) that its rim seeks the natural bony rim of the proximal end of the humerus. Small cancellous grafts are filled under the head if needed, and the replica is then tapped in solidly with a flat punch. The capsule should again be checked for loose chips lying free in the joint and such chips should be removed. The retractors are removed and the shoulder again is checked for luxation and clearance of the long head of the biceps.

The capsule is then closed with 0000 cotton interrupted sutures, the deltoid origin is sutured with 0 cotton mattress interrupted sutures, followed by routine subcutaneous and skin closure. A dry dressing is applied with a large pillow splint in the axilla, abducting the arm 70 degrees and forward flexing the arm 30 degrees. Postoperatively the first day an airplane abduction splint is substituted for the pillow splint and early ambulation is stressed. The splint is worn for three weeks. Passive exercises are begun after the third day postoperatively in all spheres above 60 degrees abduction and flexion as tolerated. After the third week active Codman exercises are begun, graduated in intensity, and followed by complete shoulder rehabilitation muscle exercises.

REMARKS

The selection of cases is limited, however, it is felt that this procedure should be considered wherever the shoulder muscles are relatively sound, where there is considerable osteocopic pain related to lesions of the bone in this area, and where greater range of motion is desired in young adults.

CONCLUSION

A case of painful aseptic necrosis of the proximal end of the humerus with degenerative joint changes, treated by a special arthroplasty is presented. Following biopsy and surgical inspection, an arthroplasty was done using a specially constructed Vitallium replica of the cartilagenous portion of the humeral head after primary excision of the pathologic tissue. The rotator cuff and accessory muscles were relatively undisturbed by surgery. A well-functioning and painless shoulder resulted.

TWO CASES OF PERFORATED INTRA-ABDOMINAL ANEURYSM COMPLICATED BY NEUROLOGICAL FINDINGS

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THE purpose of this paper is to present two instances of intra-abdominal aneurysmal perforation with resultant exsanguination, which were not diagnosed before necropsy primarily because of evidence implicating the nervous system. Both cases presented curable intra-abdominal aneurysms, but in neither was surgical treatment solicited because of signs which seemed to point directly to the nervous system.

In Case 1, the variable picture of cerebral anoxia led to an erroneous diagnosis of cerebral vascular accident. The second patient was suspected of having a brain tumor, although localizing signs were not at all definite; indeed, there was found a meningioma over the right occipital lobe, but only when a perforated aneurysm of the splenic artery brought the patient to autopsy.

CASE 1 (University Hospitals No. 802339).—A 76-year-old white man was admitted to the Neurology Service with a diagnosis of cerebral vascular accident, and died ten days later from perforation of a dissecting aneurysm of the left gastric artery.

Upon admission he was semicomatose, with flaccidity of all extremities, hyporeflexia on the right, and toe signs bilaterally. There was no choking of the optic discs. Blood pressure was 94/66; pulse, 120; respirations, 40; and temperature, 100.8° F. There was some tenderness in the upper abdomen upon deep palpation, but the remainder of the physical examination was noncontributory. Admission hemoglobin was 10.6 Gm.; lumbar puncture was normal.

Ten days prior to admission the patient had been digitalized for cardiac decompensation. Blood pressure at that time was reported to have been 230 systolic.

On the day following admission he was given 500 c.c. of whole blood and appeared generally responsive, but still confused. Blood pressure rose to 115/76. He was incontinent of feces. Reflexes were hyperactive on the right. Electrocardiogram was negative for myocardial infarction. Medications consisting of Dicumarol, digitalis, and penicillin were given. By the sixth hospital day the prothrombin time was thirty seconds, with a control of 13.5 seconds. Skull films were negative.

On the seventh day the patient was helped out of bed, but vomited, collapsed, and presented the usual signs of shock. An electrocardiogram showed some changes not present in the previous tracing, but still no evidence of infarct. Hemoglobin was now 7.6 Gm. and blood pressure 140/85. He was transferred to the Medical Service because of the possibility of coronary occlusion. No friction rub was heard.

Two hundred and fifty cubic centimeters of whole blood were given on both the eighth and ninth days after admission following which the hemoglobin was 10.2 Gm. and the blood pressure stable at 130/80. There was now less abdominal tenderness than at the time of admission, and the patient appeared to be improved.

On the tenth hospital day the patient was found in extreme shock with blood pressures of 30 and 40 systolic and the diastolic not discernible. He died shortly thereafter.

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Post-mortem examination revealed no evidence of myocardial infarction or even severe sclerosis of the coronary arteries. The brain showed only cerebral arteriosclerosis. There was moderate pulmonary edema. The peritoneal cavity was filled with 2,500 to 3,000 c.c. of recently extravasated whole blood. Examination of the vessels supplying the stomach showed a dissecting aneurysm of the left gastric artery with two large, organized hematomas on the serosal surface of the stomach. Although the exact point of extravasation was not found, it is presumed that a massive hemorrhage from the aneurysm of the left gastric artery was the terminal event. Further examination disclosed a similar dissection in the wall of the right renal artery without evidence of extravasation of blood in that area.

CASE 2 (University Hospitals No. 809972).—A 50-year-old white housewife was admitted to the Neurosurgical Service with a diagnosis of possible brain tumor, and expired three days later from massive intraperitoneal hemorrhage caused by rupture of a dissecting aneurysm of the splenic artery.

The patient had headache intermittently for two or three years with increasing severity a few months prior to admission. For two or three months she had been "run down," depressed, and lethargic. There was staggering, slow gait two weeks before admission. She became semistuporous twenty-four hours before entry to the hospital.

Temperature was 99° F., pulse 68, respirations 20, blood pressure 100/70. Examination showed a well-developed, well-nourished white woman who fell backward when standing without aid. Speech was clear but slow. There was no nystagmus or choke of the optic discs. Grasp was weak bilaterally but more so on the left. Stereognosis was unimpaired. There was no abdominal reflex, and toe signs were extensor on the right. Ankle jerks were hypoactive but bilaterally equal. The impression was that she had a supratentorial brain tumor, but there were no good localizing signs. Blood chemistries were normal, and admission hemoglobin was 14.0 Gm. Urinalysis was negative. Skull rays showed decalcification of the dorsum sellae consistent with increased intracranial pressure; the pineal was not visible. The patient was too stuporous for visual field examination.

She continued to be lethargic and became incontinent of urine. At six A.M. on the third hospital day, the day of death, the patient complained of frontal headache. There was never any evidence of abdominal pain or tenderness. Blood pressure one hour before death was 120/80, and the pulse rate varied from 50 to 80 per minute. Some coffee ground material was vomited two hours before death. Shock, then death came suddenly and without warning.

Autopsy findings were as follows: (1) meningioma over right occipital lobe; (2) hemorrhage from an arteriosclerotic splenic aneurysm; (3) fatal hemorrhage into the peritoneal cavity. There were 1,500 c.c. free blood with a large hematoma in the hilum of the spleen. The aorta and other abdominal vessels were not arteriosclerotic.

DISCUSSION

The first case manifested changing neurological findings because of cerebral anoxia. In turn, the cerebral anoxia was effected by the extravasation of blood into the peritoneal space and represented an instance of anemic anoxia. The complicating neurological findings were entirely secondary to the left gastric aneurysm. Dissecting aneurysms of the aorta frequently present neurological signs also dependent upon anoxia to both the brain and spinal cord by interference with the blood supply.[1, 2] This of course is a mechanical or physical oxygen deprivation rather than chemical. Donaldson and Hamlin have recently described three cases of gastric artery aneurysm with massive hematemesis and urge early laparotomy for undiagnosed gastrointestinal bleeding.[3] Case 1 failed to provide even this suspicion of intra-abdominal aneurysm.

Case 2 differed from the first in that a neurological lesion existed concomitantly with the splenic aneurysm. Here the neurological findings were

caused by a meningioma and not by the aneurysm. Aneurysmal rupture and exsanguination prevented the ventriculogram and craniotomy which could have ablated the neurological disease.

The literature regarding aneurysms of the splenic artery is extensive. Crisp reported the first case in 1847.[4] The aorta excepted, splenic aneurysm is the most common intra-abdominal aneurysm.[5] Few are diagnosed preoperatively; many are multiple; and the increased incidence during pregnancy is well documented.[6] The preferential sclerosis of the splenic artery to the exclusion of other abdominal vessels including the aorta is another interesting fact. Elective splenectomy whenever the diagnosis can be established is generally advocated.

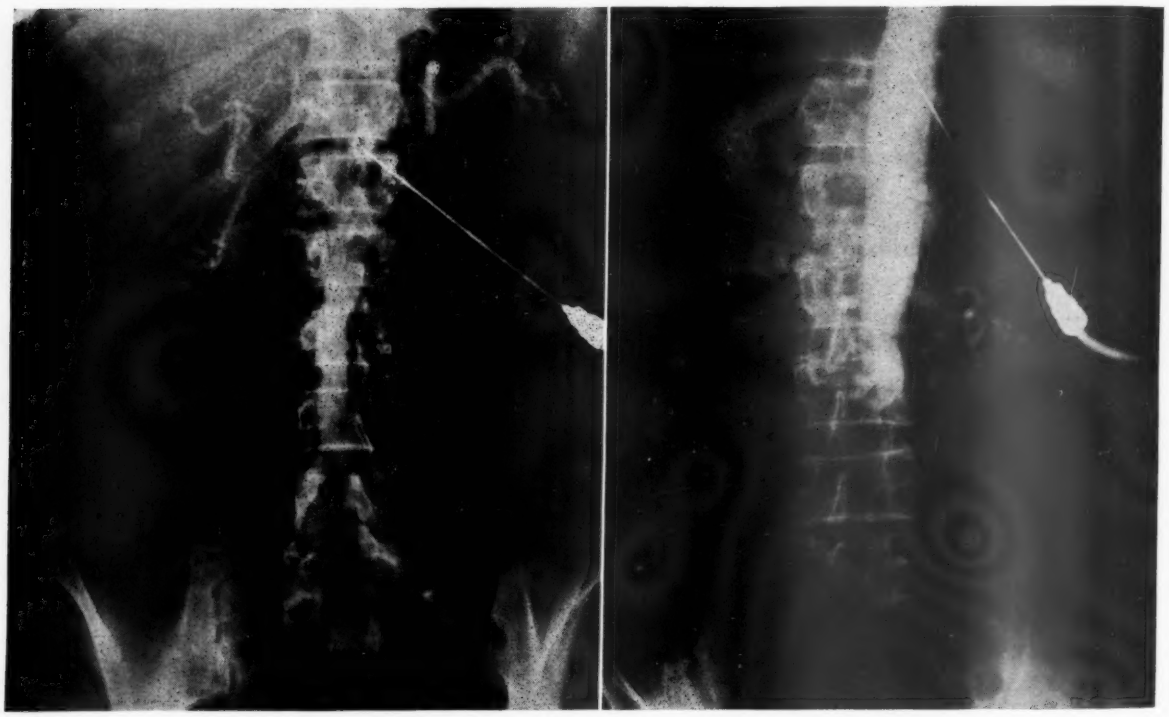

Fig. 1.—This is a normal aortogram showing especially well the tortuous course of the splenic artery (one arrow) as well as the shadow of the spleen itself (two arrows).

Fig. 2.—This is a small aneurysm of the right renal artery which was confirmed at surgery when a left hypernephroma was extirpated. This illustrates the relative ease with which intra-abdominal aneurysms may be seen by abdominal aortography.

The use of angiography of the abdominal aorta should be recommended in all instances where aneurysmal perforation is suspected in blood loss shock. Scout films of the abdomen showing calcific deposits in the region of the celiac axis and its branches should arouse suspicion of aneurysm. Given a patient with hematogenic shock and calcified material in the celiac, hepatic, gastric, or splenic arteries, an aortogram should be taken. From the experience of Donaldson and Hamlin,[3] aortography for gastrointestinal bleeding might disclose some gastric aneurysms. The problem of aneurysm of the left gastric or splenic artery is that of diagnosis, because surgical treatment is curative. Aneurysms

of the celiac axis and hepatic arteries on the other hand are not so readily amenable to surgery; however, exsanguination can be averted by surgical intervention. Grant, Fitts, and Ravdin[7] have recently reviewed their experience with aneurysm of the hepatic artery.

There will, however, always be some cases where the diagnosis is so confused that its consummation would be entirely fortuitous. Two such cases are presented here.

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CONGENITAL TRACHEOESOPHAGEAL FISTULA WITHOUT ESOPHAGEAL ATRESIA

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CONGENITAL tracheoesophageal fistula without the presence of atresia of the esophagus is a rare anomaly. This fact, associated with the difficulty of diagnosis, has been emphasized by several authors.[3, 5, 6] Haight[5] has stated that this particular condition was noted in only 3 per cent of a series of sixty-five cases of anomalies of the esophagus observed at the University of Michigan Hospital. The occurrence of this rarity in a fourteen-day-old infant, coincident with an adjacent widemouthed diverticulum of the esophagus, is reported here. Successful closure of the fistula and secondary excision of the diverticulum were performed through a left cervical incision.

CASE REPORT

M. S. (A172-099), a female infant, aged fourteen days, was transferred to St. Luke's Hospital on Sept. 14, 1949, with the diagnosis of tracheoesophageal fistula with esophageal atresia. The child had a typical history of esophageal obstruction, with immediate regurgitation after feedings associated with choking, cyanosis, and dyspnea. She had been maintained since birth on rectal and subcutaneous fluids. Roentgen studies with Lipiodol, done in another hospital, revealed that the esophagus ended in a blind pouch where a nasal catheter became arrested at the level of the second thoracic vertebral body. Since air was present in the stomach and small intestine, it was thought that the distal esophageal segment entered the trachea. Atelectasis of the right upper lobe of the lung, and extensive pneumonitis involving the right middle and lower lobes were also noted in the roentgenograms.

On the day following admission, the child was very dyspneic and slightly cyanotic. She was esophagoscoped, and, under fluoroscopic control, a catheter was passed easily into the stomach, demonstrating continuity of the esophagus. However, a second, smaller catheter, inserted alongside the first, was seen to lodge in a blind pouch at about the level of the second dorsal vertebra. Lipiodol, introduced into the catheter arrested in the pouch, outlined what appeared to be an esophageal diverticulum projecting to the left of the midline. When the contrast medium had filled the sac, it flowed around the first catheter, and entered the stomach, revealing the distal segment of the esophagus to be patent, and normal in size (Fig. 1). After the catheters had been withdrawn, it was noted that the Lipiodol had entered the tracheobronchial tree. This was thought to be due to regurgitation and aspiration (Fig. 2). No tracheoesophageal fistula was demonstrated, although examination of the infant was not conducted in the prone position as advocated by Haight.[5]

Believing that the diverticulum was responsible for the infant's syndrome of excessive salivation, and attacks of choking, dyspnea, and cyanosis, a Stamm gastrostomy was performed under local anesthesia on Sept. 20, 1949. Following this procedure, the child continued to remain in poor condition. She failed to gain weight, despite adequate caloric intake via the gastrostomy, and had to be maintained in an oxygen tent with repeated pharyngeal suction. Serial roentgen studies of the lungs showed progressive atelectasis of the right upper lobe, and increasing pneumonitis of the remaining lobes of the lung (Fig. 3). Because of the lung pathology, it was felt that operative repair of the diverticulum was indicated.

On Nov. 28, 1949, sixty-one days following gastrostomy, the esophagus was exposed through a left cervical incision, under local anesthesia. The sternomastoid muscle and carotid

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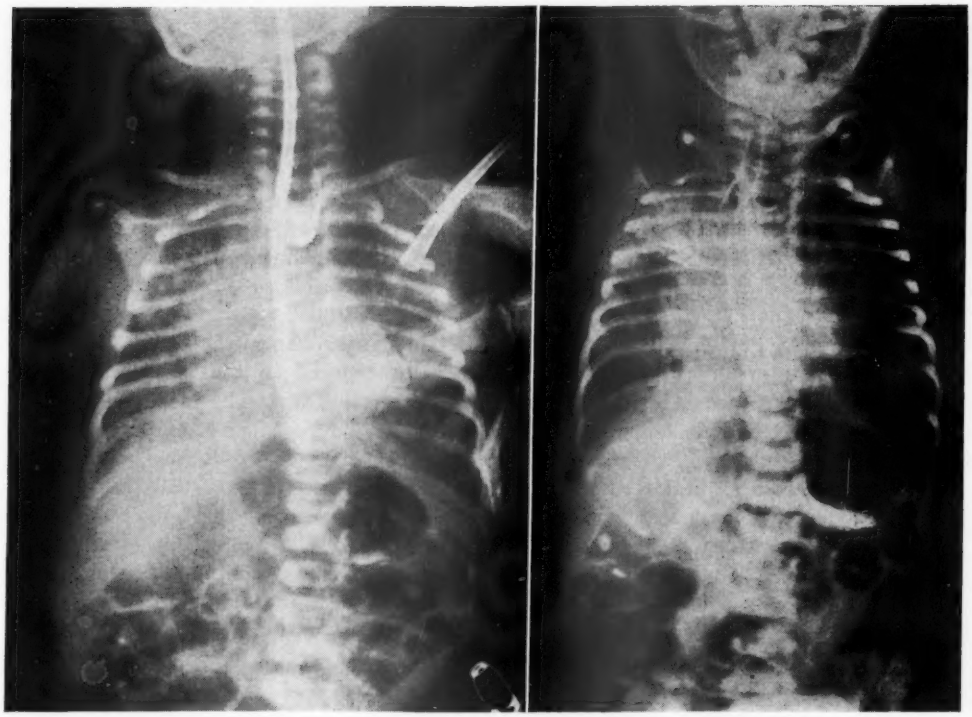

Fig. 1. Fig. 2.

Fig. 1.—Roentgenogram showing catheter outlining length of esophagus down to cardia, with Lipiodol-filled diverticulum present to the left of the midline. Note pneumonitis of right upper lobe of lung. Air and Lipiodol present in stomach.

Fig. 2.—Roentgenogram taken following withdrawal of catheter. Contrast medium fills the tracheobronchial tree, and is present in stomach. Note atelectatic right upper lobe of lung with tracheal deviation.

Fig. 3.—Chest roentgenogram on Nov. 22, 1949, indicating widespread pneumonitis involving right lung.

sheath were retracted posteriorly, and the esophagus visualized. A pouchlike, widemouthed diverticulum of the esophagus, which closely simulated the blind upper segment seen in the common type of atresia cases, was found lying just to the left of the midline. Further exploration of this area revealed a fistula between the trachea and esophagus, measuring 1.8 cm. in diameter, arising at a point directly opposite the esophageal sac. The fistula entered the posterior wall of the trachea 2 cm. proximal to the carina (Fig. 4). The fistula was divided, and the ends closed with a single layer of interrupted 000 chromic catgut sutures (Fig. 5). A No. 12 French nasal catheter was left in the esophagus, the pouch was partially invaginated with interrupted sutures of chromic catgut placed in the muscularis, and the cervical incision was closed in layers around a small Penrose drain. The infant withstood the procedure well. A transient esophageal fistula developed in the wound on the fourth postoperative day, but this closed spontaneously on the twenty-fifth day following operation. The baby was then started on oral feedings, and within a week was receiving all the formula by mouth. Postoperative chest roentgenograms showed improvement of the lung condition, and barium studies carried out on the thirty-seventh postoperative day proved the esophagus to be patent, and unobstructed. The gastrostomy tube was removed on the following day, and the child was discharged on the forty-fifth postoperative day (one hundred fourteenth hospital day) much improved.

At home, however, the child almost immediately experienced difficulty in taking her feedings. The symptoms of coughing, regurgitation, and dyspnea with each feeding recurred, and she was readmitted after one week at home. At this time, the lung fields appeared clear by roentgen examination, but coarse, moist râles were heard over the entire right lung posteriorly. Repeat barium studies of the esophagus, done on Jan. 30, 1950 (Fig. 6), again showed enlargement of the cervical esophagus, and most of the contrast medium filled the pouch with only a small portion entering the distal esophagus. Under local anesthesia, the gastrostomy tube was replaced on Feb. 2, 1950, and tube feedings were substituted for oral feedings. This regime was maintained for ten months with gradual weight gain, and general improvement. During this period the child had many upper respiratory infections which, however, responded to antibiotics.

On Dec. 15, 1950, the esophagus was exposed under endotracheal anesthesia via the original left cervical incision. The sternomastoid muscle was retracted posteriorly, and the esophagus, with the pouchlike segment, was mobilized from its bed. The pouch was opened on its left lateral surface, and its lumen examined for any residual fistulous connection with the trachea, and none was found. The redundancy of the sac was excised, and the esophagus was closed with two layers of interrupted chromic catgut around a No. 12 French nasal catheter. A small Penrose drain was led down to the muscle. The child withstood the operative procedure well. A fistula, with a mucous discharge, developed in the wound on the third day following operation, but this closed by the eighth postoperative day.

The child was started on oral feedings on the twelfth day following operation. She swallowed solids and puréed foods without any trouble, but, for about two months, she experienced considerable difficulty with fluids. Apparently the child had to re-educate herself to swallow rather than aspirate ingested liquids. Improvement proceeded rapidly thereafter, and when she was discharged on March 3, 1951, fluids were being taken without difficulty. Follow-up Lipiodol studies, and esophagoscopy revealed some angulation of the cervical esophagus in the operative region, but no stenosis or dilatation was noted.

DISCUSSION

The first successful surgical repair of this anomaly was reported by Imperatori,[6] in 1939. His patient had remained undiagnosed until the age of 6½ years. The fistula was exposed through a midline tracheotomy incision, and closed by suture. The second successfully treated case was a patient of Haight's,[5] whose diagnosis was not established until he was 4 years of age. A retropleural approach was employed in this child, and the fistula, which entered the trachea

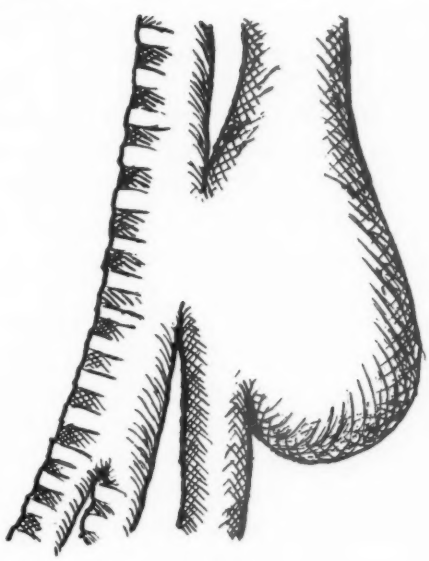

Fig. 4.

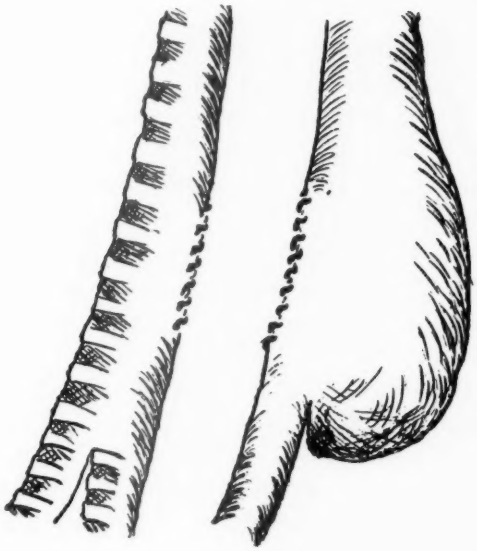

Fig. 5.

Fig. 4.—Drawing of anomaly illustrating tracheoesophageal fistula 2.5 cm. proximal to the carina, with patency between the esophageal segments.

Fig. 5.—Illustration showing division of the fistula, with closure of the trachea and esophagus with interrupted sutures. Secondary operation excised esophageal pouch.

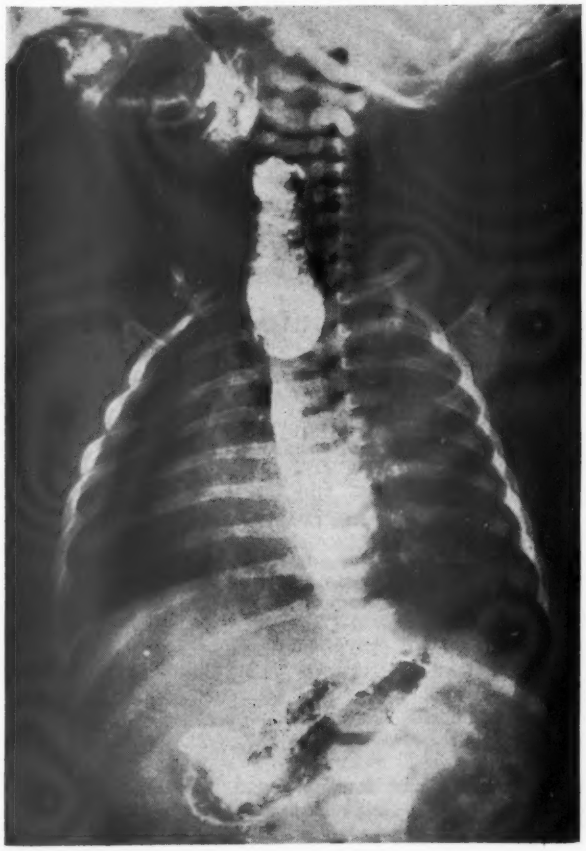

Fig. 6.—Barium studies of esophagus taken on Jan. 30, 1950, after admission for recurrence of symptoms. Size of esophageal pouch has increased.

2.5 cm. proximal to the carina, was divided in the posterior mediastinum. Gross[4] recently has successfully divided and closed the fistula in three cases.

Surgeons with wide experience in this field have not reported a case where the fistula, not associated with atresia, was further complicated by a pouchlike diverticulum of the esophagus arising in the region of the fistula. Brintnall and Kridelbaugh[1] have recently reported two cases of congenital esophagopharyngeal diverticula which were originally diagnosed as esophageal atresia. These patients were explored through the retropleural space, and what was thought to be the proximal blind esophageal pouch in each case was a large diverticulum. The esophagus was normal, and there was no evidence of tracheoesophageal fistula in either infant.

The case described here is the first of its type recorded in the history of St. Luke's Hospital. Although it cannot be classified with any particular category of Ladd's[7] classification of congenital esophageal anomalies, it most closely resembles those in Type III. Since the esophageal pouch, diagnosed originally as a diverticulum, so closely simulates the proximal blind esophageal segment seen in 90 per cent of the atresia cases, it may be suspected that this child's anomaly represents an arrest somewhat later in the course of development of the esophagus and trachea. As shown in Fig. 5, the only difference between this case and the classical type of atresia is the persistence of the blind end of the upper segment in spite of actual continuity between upper and lower segments.

It is remarkable that the child survived for two months following the gastrostomy with such a large fistula, and so much insult to the right lung from repeated aspiration, both from the upper pouch, and from the stomach. It is also fortunate that the fistula entered the trachea high enough to be exposed, and divided through the incision in the left cervical region, which had been planned originally for a diverticulectomy. This case further emphasizes the difficulty of diagnosis of these fistulas when there is no esophageal atresia.

SUMMARY

1. An unusual case of tracheoesophageal fistula treated surgically with successful outcome is reported.

2. The difficulty of diagnosis of this type of anomaly, when not associated with esophageal atresia, is emphasized.

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SPONTANEOUS GASTROJEJUNOSTOMY

Report of a Case

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SPONTANEOUS gastrojejunostomy is an extremely rare occurrence. Reports of spontaneous ileoileostomy, ileocolostomy, and gastrocolostomy have occasionally appeared,[4] and gastrojejunocolic fistulas secondary to surgical gastroenterostomy or malignancy are frequently encountered.[1, 3, 6, 7] Careful review of the literature has revealed only one report of a case of spontaneous gastrojejunostomy, that by Horner and Kenamore in 1940.[5] These authors reported one case of their own and stated that a review of the literature up to 1923 revealed no other cases. Because of the rarity of this condition, we believe that our case warrants publication.

CASE REPORT

R. E. K. (R-96 115), a 55-year-old white man, was in good health until 1931, at which time he contracted syphilis. He received antiluetic treatment, and remained in fairly good health until 1945, at which time he was admitted to the Huntington Veterans Hospital complaining of weakness, vague stomach trouble, and nervousness. Physical and laboratory findings at that time were diagnostic of tabes dorsalis. While he was in the Huntington Hospital, an upper gastrointestinal series was obtained on April 12, 1945, which was reported as normal. He was transferred shortly thereafter to the Dayton Veterans Administration Center for domiciliary care.

He was admitted to Brown General Hospital, Dayton Veterans Administration Center, on Jan. 18, 1951, because of an anemia noted in a routine domiciliary physical examination. Three or four months prior to admission he had been told by his associates that he appeared pale. Concomitantly, he had complained of mild episodes of nausea and vomiting coming on immediately after eating. The vomitus consisted of recently ingested foods; it contained no bile or feces. There was no associated epigastric or abdominal pain. On the day prior to admission, the patient for the first time noted one large, tarry, well-formed bowel movement. He had had no constipation, diarrhea, or hematemesis.

Physical Findings.—Physical findings on admission revealed a pale, anemic white man, with a blood pressure of 126/40. The pupils were fixed, unequal; the left smaller than the right. The mucous membranes appeared pale. The cranial nerves were intact. There was no abdominal tenderness or rigidity; no abdominal masses were present. Liver, kidneys, and spleen were not palpable. The bowel sounds were 10 to 20 per minute, the pitch being normal. Rectal examination revealed a diminished sphincter tone. No hemorrhoids or masses were palpable. Examination of the genitalia revealed a chancre scar on the glans penis. Neurological examination confirmed the diagnosis of tabes dorsalis.

Laboratory Findings.—Laboratory findings were: red blood count 2,720,000, hemoglobin 6.5 Gm., white blood count 15,750, neutrophils 75 per cent. Prothrombin time on admission was 80 per cent of normal. Sedimentation rate was 16 mm. per hour; hematocrit was 21

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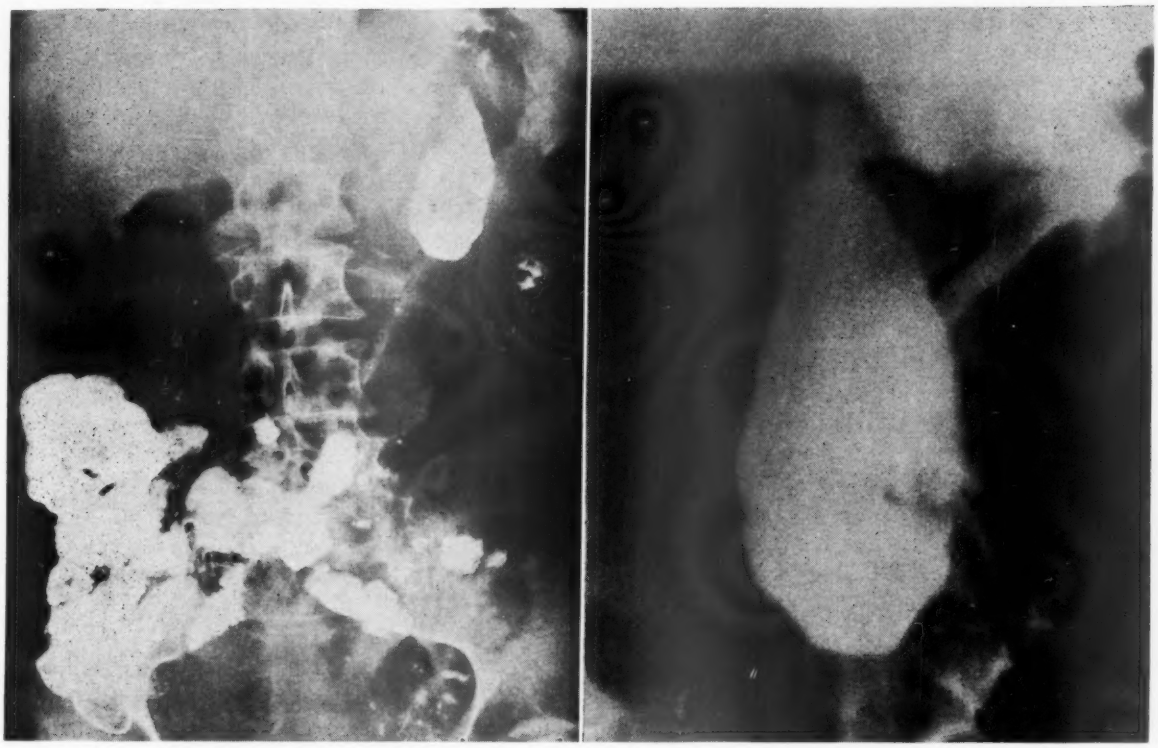
volumes per cent. Blood indices on admission were: mean corpuscular volume 93, mean corpuscular hemoglobin 26.6, mean corpuscular hemoglobin concentration 28.5. Examination of the red cells revealed an associated anisocytosis, polychromasia, and slight hypochromia. Admission urinalysis revealed 15 to 20 white cells per high power field, but was otherwise negative. Gastric analysis performed Jan. 16, 1951, revealed a low hydrochloric acid with no acid present in the first two specimens, 10 degrees hydrochloric acid present in the third specimen, and 22 degrees free hydrochloric acid present in the fourth specimen. The total acidity ranged between 18 and 46 degrees. Examination of the stool for occult blood ranged between 2+ and 4+ on all occasions. Repeated red cell and hemoglobin determinations consistently revealed a hypochromic anemia. Serology reported Kahn 4+, Kline 3+, and Wassermann 3+. Roentgenologic examination of the thorax on Jan. 17, 1951, showed an accentuation of the bronchovascular markings bilaterally; the lung fields were otherwise essentially clear.

Fig. 1.—There were two visible gastric ulcers; one was a large penetrating ulcer on the posterior wall which measured approximately 6 cm. in its greatest diameter, and through this on the posterior wall was seen another niche with radiating folds which was also in the pars media on the posterior wall.

The heart was of normal size but there was some elongation and tortuosity of the aorta. Fluoroscopic and radiographic studies of the upper gastrointestinal tract showed the esophagus to be completely normal. The stomach was definitely hypotonic and was J-shaped. A large ulcer crater measuring approximately 1½ cm. in its greatest diameter was located on the lesser curvature in the posterior wall at the pars media of the stomach, and showed multiple radiating folds out from this area. Just above this, also on the posterior wall, was a huge penetrating ulcer measuring 5 to 6 cm. at its base. The duodenal cap was large and showed no irregularities or evidence of spasticity. There was approximately 25 per cent gastric retention at the end of six hours. The six-hour film showed a large barium-filled area in the region of the large ulcer crater which represented residual barium contained within the ulcer. These findings were confirmed by re-examinations on Jan. 25, 1951. In addition, the six-hour film showed the larger ulcer crater to be filled with barium. There was a radiolucent area in the center of the ulceration. In retrospect, this may have represented the point of perforation into the jejunum. Gastroscopic examination performed Jan. 23, 1951, showed a large ulceration with clearly demarcated edges and radiating folds, with no evidence of

nodulation. The exact depth of this ulcer could not be ascertained with the gastroscope; however, it appeared to be grossly benign. The edge of the second ulcer was poorly visualized on the lesser curvature.

Course in Hospital.—The presumptive diagnosis was two large, probably benign, gastric ulcers; however, the possibility of gastric syphilis was entertained. For the latter reason the patient was placed on a course of penicillin therapy, being given 6,000,000 units. Following this therapy there appeared to be no change in size and configuration of the ulcer. Therefore, following preparation of the patient with a total of 5 units of blood, which elevated his hemoglobin to 13.6 Gm. and his red blood count to 4.3 million, he was subjected to surgery on Feb. 27, 1951.



A. *B.*

Fig. 2.—The six-hour film showed the large ulcer crater to be filled with barium. A radiolucent area was evident in the center of the ulceration. In retrospect, this may have represented the point of perforation into the jejunum.

Pertinent Operative Findings.—Through a left rectus incision extending from the xiphoid process to a point 1 inch below the umbilicus, the abdominal contents were exposed. There was no free fluid in the abdomen. The liver appeared red-brown in color, had a smooth edge, and showed no evidence of macronodular cirrhosis or metastasis. Kidneys, spleen, gall bladder, large and small bowel appeared normal to gross examination. There were numerous soft, pinkish nodes along the gastric vessels. These varied in size from 1 to 3 cm. in length and all measured approximately 0.5 cm. in width. Examination of the stomach itself revealed a large penetrating ulcer in the middle third of the stomach on the posterior wall. This ulcer measured approximately 3 by 5 cm. in diameter. The duodenal bulb appeared normal. Because of the necessity of performing a high resection, the left coronary ligament of the liver was transected and the left lobe of the liver retracted to the right. Gastric vessels were isolated, the duodenum transected in its first portion, and the duodenal stump closed. Following ligation of the left gastric artery near its origin, the stomach was elevated. At this time it

was found that the large, posterior ulcer previously described had penetrated into the transverse mesocolon and pancreas to a considerable depth. Because of the size of this ulcer it was impossible to excise it. Therefore, the stomach was entered about the margins of the ulcer and the base of the ulcer exposed. This ulcer had penetrated through the posterior wall of the stomach into the lesser peritoneal sac, coursed along the posterior peritoneal layer of the lesser sac, extended over the anterior border of the body of the pancreas, penetrated the transverse mesocolon to the left of the middle colic vessels, and perforated into the first portion of the jejunum approximately 5 cm. from the ligament of Treitz. An elliptical opening in the jejunum measuring 2 cm. was found. As it was exposed, the jejunal mucosa puckered through this opening. No evidence of marginal ulceration was noted about this area. The wall about the jejunal perforation appeared thickened and fibrotic. The stomach was freed from adhesions in the lesser sac and two Carmalt clamps applied high on the stomach. The stomach was transected between clamps 5 cm. proximal to the edge of the ulcer. The edges of the jejunal perforation were excised and the opening was closed transversely with a series of 000 interrupted silk Halsted mattress sutures. A posterior Hofmeister-Finsterer antiperistaltic subtotal gastrectomy was performed. The patient's postoperative course was uneventful. He was placed on Levine suction for three days postoperatively. He was given 1 ounce of water every hour on the fourth day, clear liquids by the sixth day, and a four-feeding Meulengracht diet by his seventh postoperative day. The sutures were removed on the tenth postoperative day. Wire stay sutures through the anterior rectus sheath were removed on the fourteenth postoperative day. The wounds healed per primam. Since surgery the patient's course has been uneventful.

Pathologic Findings.—Pathologic examination revealed a large portion of the stomach which measured 18 cm. along the lesser curvature and 33 cm. along the greater curvature. On the posterior wall there was a large gaping defect measuring 5½ cm. in diameter. The edges of the defect remained indurated and slightly elevated and congested. This represented the area of penetration of the large posterior ulcer. A second smaller ulcer measuring 1 cm. in diameter was found 3 cm. distal to the first ulcer. It was covered with mucus and showed some evidence of healing. Microscopic examination revealed that both ulcers were benign and there was no evidence of gastric syphilis.

Comment.—Although fistulas between the stomach and colon, and between the stomach and duodenum are relatively common because of the contiguity of these viscera, a fistulous communication between stomach and jejunum is rare. Such a communication is possible only when a previous inflammatory reaction within the lesser sac has bound the posterior wall of the stomach to the posterior peritoneal area of the lesser sac. The process then must extend over the anterior border of the body or tail of the pancreas and erode through the transverse mesocolon into the jejunum. In their report, Horner and Kenamore[5] postulated the possibility of a jejunal herniation through a congenital rent in the transverse mesocolon. There was nothing to suggest that this was an etiological factor in our case.

The diagnosis of gastrojejunal fistula was not made prior to surgery in this case because of the failure to demonstrate it by roentgenogram and gastroscopy. It was felt that the superimposition of the stomach and the colon upon each other and upon the lesion itself obscured roentgenological visualization of the fistula. It is doubted that the entrance of the fistula into the jejunum could be visualized by gastroscopy because the length of the tract would have obscured the jejunum. In the case reported by Horner and Kena-

more[5] the lesion was demonstrated prior to surgery by roentgenography and gastroscopy. The pyloric location, patency of fistula, and lack of superimposition of adjacent structures facilitated its demonstration.

Although our patient was tabetic, gastric lues was not diagnosed. Luetic involvement of the stomach is usually manifested by palpable mass, roentgenologic findings simulating neoplasm, or an hour glass stomach where the process is diffuse and involves both walls. Moreover, there is usually a dramatic response to any antiluetic medication. None of the above was applicable to our case. It is interesting to note that this patient had a normal gastrointestinal series five years prior to admission. The development of ulcers in this patient conforms to Crohn's[2] concept that lack of motility in the tabetic is a factor in the etiology of peptic ulcer. This patient's paucity of symptoms may well be explained on the basis of his central nervous system disease.

CONCLUSION

A case is reported of a 55-year-old white man with tabes dorsalis in whom two gastric ulcers were found. The larger penetrated through the posterior gastric wall, extended along the posterior peritoneal layer of the lesser sac, over the tail of the pancreas, and eroded through the transverse mesocolon. It then penetrated into the jejunum near the ligament of Treitz, causing a spontaneous gastrojejunostomy.

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Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

THE PATHOGENESIS AND CLINICAL MANAGEMENT OF MEGACOLON WITH EMPHASIS ON THE FALLACY OF THE TERM "IDIOPATHIC"

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ADVANCES during the past five years have brought about a marked revision in previous concepts of the etiology and management of megacolon. Actually the information necessary to the solution of the megacolon problem has been available for over twenty years, but the original misconception of Hirschsprung, and his influence on subsequent observers, makes it difficult even now to dislodge the firmly entrenched notions which he unwittingly implanted. The years of confusion and empiricism in the diagnosis and management of megacolon are not a credit to the medical profession. With data now at hand the pathogenesis of megacolon need no longer be a mystery and the term "idiopathic" has no application. The purpose of this paper is to demonstrate the tenability of this thesis by analysis of the available facts and to illustrate it by representative case reports.

It is unfortunate that in his classic description of two autopsy cases, Hirschsprung[12] should have been preoccupied with the dilated and hypertrophied colon. He mentioned casually and incidentally the fact that the rectum was not dilated and seemed to be slightly narrowed. His discussion centered on the marked hypertrophy of the bowel wall, especially of the muscular layers, the inflamed and edematous mucosa, the ulceration, and the submucosal abscesses. It is difficult to understand how the true significance of all this could have been missed but judgment is tempered by the realization that it continued to be missed by scores of able clinicians for well over half a century.

It is interesting that Sir Frederick Treves[29] of London, one of the leading British surgeons of his time, very nearly solved the problem within a year of Hirschsprung's report, and probably before he had heard of the latter's paper. In a case of "Idiopathic Dilatation of the Colon" he did a colostomy and noted that the process receded markedly. The colostomy did not function well and finally he performed a counterpart of Swenson's operation, except that he did not preserve the sphincter. To anyone who has had experience with an uncontrolled perineal colostomy, the reason that Treves' operation was not widely accepted will at once be apparent. Had Treves been able to preserve the sphincter and had he recognized the reason for the otherwise excellent result in his patient, the problem of megacolon might have been solved before the turn of the century.

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Report after report can be found in the literature where patients with megacolon have been restored to good health by colostomy, only to return to their previous condition if the colostomy was closed. Writer after writer has commented on the fact that infants with "congenital dilatation and hypertrophy of the colon" can be improved *if the enema tube is introduced very high* and repeated enemas given in this way. If this treatment was discontinued or improperly performed, the infants died of obstructive symptoms. Over and over again surgeons resorted to resection of part or all of the colon, *except the terminal segment,* and anastomosed the proximal bowel to this same "normal" segment. The patients were improved for a time, but sooner or later the process of dilatation and hypertrophy would recur. There were some exceptions, but the reason for them was not apparent because there was no workable basis for the separation of one type of megacolon from another.

All of these observations could mean but one thing: namely, that the colon was the seat of chronic, incomplete obstruction, but for reasons which we shall attempt to make clear, their significance was misinterpreted.

It is common knowledge that chronic incomplete obstruction of any hollow viscus produces dilatation and hypertrophy, especially of the muscular coats, above the level of the obstruction, that the degree and extent of the hypertrophy depend upon the degree and duration of the obstruction, and that obstructive hypertrophy and dilatation result in an increase in both length and diameter of the obstructed viscus. If to this is added the erosive and inflammatory effect of prolonged fecal impaction, then the entire natural history of the disease becomes clear. Once it is recognized that obstruction from one cause or another is always present, it remains only to determine what is producing the obstruction and to treat the case accordingly.

The greatest stumbling block to a proper interpretation of the observed facts has been that in so many cases no recognizable organic obstruction could be demonstrated. That form of megacolon secondary to obstructing stricture or tumor has long been recognized and has been termed symptomatic or organic megacolon. It has never presented any problem, and yet the pattern is so similar to that of the so-called "idiopathic" type that, in retrospect, it seems almost incredible that the latter could have been attributed by so many distinguished observers, including Hirschsprung, Osler,[16, 17] and Finney,[8] to a disorder intrinsic within the dilated and hypertrophied bowel itself. If such an interpretation were correct, it would represent the only instance known to medical science of a hollow viscus becoming chronically dilated and *hypertrophied* in the absence of obstruction. The acute distention of paralytic ileus and related conditions is another matter entirely.

In seeking the location of an obstruction, the surgeon or pathologist follows the dilated bowel down to the point of narrowing and here the obstruction is to be found. Although many observers have postulated that obstruction must be present, it was attributed to redundancy and kinking or volvulus of the elongated bowel or to similar mechanisms, and several essential features were ignored. These are, first, that in most of these cases the ob-

structive symptoms begin at birth and recur even when the excess bowel is removed, and second, that elongation is part of the physiologic effect of chronic incomplete obstruction of any tubular viscus.

In spite of these two important facts, the narrow terminal segment seen in true Hirschsprung's disease was dismissed as "normal," because it appeared grossly to be normal and a rectal tube could always readily be passed through it for temporarily effective, decompressive enemas. Only comparatively recently has there been any consistent study of the ganglion cells of Auerbach's and Meissner's plexuses in the "normal" terminal segment in cases of true Hirschsprung's disease. In reviewing the literature we find a total of seventy-six cases, including our own, conforming to the diagnosis of aganglionic megacolon, in which the terminal segment has been subjected to microscopic study. In every case where ganglion deficiency has been sought, it has been found.

So far as we are able to determine, credit for the first recognition of the etiology of true Hirschsprung's disease should go to Dalla Valle[4] of Parma (1924) and Cameron[3] of Glasgow (1928).* The former described two autopsy cases in brothers, and suggested that absence of ganglia in the terminal segment might be present in other similar cases. Cameron, who probably had not heard of the Italian report, and based his study on previous work of his own on achalasia of the esophagus, also reported two autopsy cases of Hirschsprung's disease and definitely proposed that the aganglionic segment was the cause of the disorder in his and similar cases. He believed that the ganglia had been destroyed by an inflammatory process. Although the present belief is that the deficiency is congenital, for practical purposes it makes little difference whether the ganglion deficiency is due to agenesis or whether it results from an inflammatory process in utero. To this extent Hirschsprung's closing statement was true when he said, "If one takes into consideration the fact that the difficulty with defecation begins with life itself, it seems highly probable that the basic disease, brought from the womb, must either be ascribed to a congenital anomaly or to a morbid fetal process." Unfortunately Hirschsprung was referring to the dilated bowel rather than to the real location of the disease. The fact remains that Cameron recognized the functional obstruction resulting from parasympathetic ganglion deficiency antedating the report of Robertson and Kernohan[21] by ten years. These writers, quoting Lendrum's work on achalasia of the esophagus as their stimulus, rediscovered the aganglionic condition of the terminal segment in 1938. In 1948, Whitehouse and Kernohan[30] expanded this initial report with eleven additional cases. Meanwhile, the work of Zuelzer and Wilson,[31] Swenson and co-workers[24] began to emphasize the significance of the achalasic or aganglionic segment. Swenson, in a modification of a principle published by Ravitch[18, 19] in 1947, devised an operation for removing the obstructing terminal segment without destroying the anal sphincter. His results were dramatic and have done perhaps more than anything else to provide a solution to the megacolon problem. This tremendous forward step was followed by the report of Bodian, Stephens, and

*Tittel[28] in 1901 had postulated a possible relationship to ganglion deficiency but his report is equivocal and inconclusive and his microscopic study did not include the rectum.

Ward[2] whose careful analysis of seventy-three cases of "idiopathic" megacolon pointed the way toward a rational method of selective diagnosis and treatment. Hiatt's[10] very recent report represents a major contribution to a clearer understanding of the pathologic physiology of true Hirschsprung's disease. His correlated interpretation of kymographic tracings from balloons implanted in the bowel with microscopic examination of the resected segments throws a great deal of light on the mechanism of the obstructive process. Nevertheless, a strong tendency has remained to cling to the old approach to the problem and to attribute the dilatation and hypertrophy of the colon to some mysterious disorder within the enlarged portion itself.[9, 20] For many years it has been recognized that an autonomic imbalance was present, but its anatomic location remained a mystery because it was sought for everywhere except in the most obvious place—the point of obstruction. The literature on this phase of the problem has been summarized in a previous publication and need not be repeated here.[15] Suffice it to say that the reason for the autonomic imbalance in true Hirschsprung's disease has been amply demonstrated and all that remains a problem is to differentiate patients who have an aganglionic segment from those who do not, and treat them accordingly. Herein lies the importance of differential diagnosis, for all cases of megacolon are not true Hirschsprung's disease, and unless this fact is recognized, treatment may be dangerously misapplied. Even very recent comment fails to emphasize the importance of differential diagnosis.[6] The present discussion seeks to clarify the problem and to supplant the classification previously given.

ETIOLOGY OF MEGACOLON

It must be recognized at the outset that the colon differs in no way from any other living hollow viscus through which a stream of contents must be moved. If it becomes acutely and completely obstructed, massive dilatation without hypertrophy results. If obstruction is unrelieved, death ensues. If the colon is chronically and incompletely obstructed, dilatation and hypertrophy are the result. When impaction of feces above the level of obstruction is allowed to persist, pressure necrosis, infection, and ulceration follow. If the impaction renders the obstruction complete enough to be inconsistent with survival, the patient dies as surely as he would of intestinal obstruction from any other cause. In every case of megacolon it is essential only to recognize that obstruction is present and to seek and correct its cause. On this basis the condition readily falls into three general categories.

THREE TYPES OF MEGACOLON

1. Achalasic or Aganglionic Megacolon (True Hirschsprung's Disease).—Achalasic megacolon presents a strikingly different pattern from the two other types of megacolon subsequently to be described, and until the absence of parasympathetic ganglion cells in the terminal segment was demonstrated, they were largely responsible for the mystery of megacolon. No one found anything wrong with the terminal segment and no one, before Dalla Valle[4] and

Cameron,[3] could believe that a segment of bowel which looks and feels normal could produce obstruction. Recognition of the fact that the parasympathetic ganglia are deficient in this segment explains the functional obstruction. As Hiatt has shown, a type of mass contraction can and does occur in it, but no orderly peristaltic wave, and although the bowel appears to be grossly normal, the functional obstruction of achalasia can be proved to be present. Since the fecal stream at the terminal level has undergone maximal water absorption and is semisolid, an uninterrupted and effective peristaltic wave is even more essential to its passage here than it might be in those parts of the bowel where the content is liquid. Fortunately, the ganglion deficiency nearly always involves only the lower rectum and sigmoid. In one of Zuelzer and Wilson's[31] eleven cases, the deficiency extended up into the ileum to a point 22 cm. above the ileocecal valve. In Tiffin, Chandler, and Faber's[27] case the ganglion deficiency was apparently segmental with normal ganglia both above and below. These two cases are rare exceptions. Nearly always the achalasic segment starts at the anus and extends for a variable distance up the left colon, usually only into the sigmoid.

Regardless of the level to which the ganglion deficiency extends, it is here that the obstructive process lies, and the bowel is dilated and hypertrophied above it. This fact is responsible for one of the characteristic features of aganglionic megacolon, namely, that the dilatation rarely extends all the way to the anus. Hiatt[11] has shown that the dilatation may extend to the anus in an occasional case of achalasic megacolon, but in the vast majority of cases the dilatation ends well above the pelvic floor and distal to this the bowel appears normal or slightly narrowed. This situation is usually demonstrable both clinically and radiologically. From a clinical standpoint, the digital and sigmoidoscopic examination may be virtually diagnostic. In functional megacolon, the examining finger finds a large mass of impacted feces in a widely dilated lower rectum. When the impaction has been removed, the dilatation is still apparent by both methods of examination. In contrast, the rectum looks and feels normal in nearly all cases of aganglionic megacolon. While there may be in the rectum a small amount of hard stool which has worked its way down from the level of obstruction and major impaction, it is quite different from the massive impaction in the lower rectum found in organic or functional megacolon. When the bowel has been cleansed, the rectum appears normal to both digital and proctoscopic examination.

The radiographic picture is also characteristic in the well-advanced case, that is, when the megacolon is well established and has not been decompressed by early colostomy. The reasons that confusion in radiologic interpretation may occur will be discussed later. For the present, it can be stated that when the full-blown picture of megacolon is present, the dilatation only rarely extends all the way to the anus and nearly always terminates at a higher level with a terminal segment of normal-looking bowel below it. Examples of this situation were illustrated in a previous paper.[15]

Before pursuing the objective findings in the differential diagnosis, the essential feature characteristic of aganglionic megacolon should be emphasized. This is the history and clinical course, which should lead one to the diagnosis. In contrast to either symptomatic or functional megacolon, *the onset of obstructive symptoms is at birth or within the first few days thereafter.* In reviewing the published cases, including Hirschsprung's original two, and in our own experience, this feature is consistently present. As indicated in the foregoing section, the question of whether the ganglion deficiency is due to agenesis or to an intrauterine process is largely academic. The answer to this question would complete the solution of the "megacolon problem" and if the lesion could be shown to be inflammatory or acquired, some means of preventing it might be found. But this question is not pertinent to the differential diagnosis. The important points are: first, that the onset of obstructive symptoms is early and persistent; second, that morbidity and mortality from episodes of acute obstruction are high; the third, that the obstruction can be relieved temporarily, but never permanently, by conservative measures.

These features in the history, together with the radiographic findings, when these are properly interpreted, permit the diagnosis to be made with a high degree of certainty.

The fact that the symptoms begin so early might lead one to suppose that the distinction between megacolon and the several gross congenital obstructions might be difficult to make. Actually this is not the case, because such defects as atresia at any level or meconium ileus produce *complete* acute obstruction which cannot be relieved by enema. When such acute complete obstruction is present, a barium enema reveals a microcolon which is virtually diagnostic of complete congenital obstruction.[7, 14] Where partial obstruction is due to bands, kinks, or midgut volvulus (rare in the newborn infant), no relief is obtained by conservative measures, and a flat film is of great value in estimating the level of obstruction from the distribution of the gas-filled loops. In early true Hirschsprung's disease, except possibly in the unusual situation of Zuelzer and Wilson's[31] case mentioned previously, the obstruction is incomplete and can nearly always be relieved in young children by enemas and laxatives, provided the enema is given high enough. As soon as such treatment is discontinued, the distention and signs of obstruction recur. With proper attention to these measures, vigorously and regularly administered, these infants can in most cases be carried along in a good state of health until a favorable time for surgical intervention can be chosen. In older patients who have survived long enough for the disease to be well advanced, it may not be possible to effect adequate decompression with enemas. In these cases, however, the radiographic picture is characteristic, and will readily confirm the diagnosis. Their management is discussed later.

It is important to realize that the earlier the case is seen and the more conscientious the medical management has been, the more equivocal the radiologic findings will be. It is obvious that if effective decompression has been provided, especially in very young infants, the dilatation of the colon above

the achalasic segment will not have had a chance to develop to any very pronounced degree. The striking difference between the dilated segment and the terminal segment will not be present as it is in more advanced cases. The radiographic picture will, therefore, be atypical and a definitive demonstration of the lesion may be difficult to achieve. Moreover, although we have not encountered such a situation, the occasional case of true Hirschsprung's disease, mentioned by Hiatt,[10] in which the dilatation extends all the way to the anus, might confuse the radiographic interpretation. In our experience and in that of others,[2, 5] a radiographic diagnosis can usually be made, though often only after repeated attempts, by careful fluoroscopic control, and spot films, in the course of which a consistently narrow segment can be seen somewhere in the sigmoid.

Even when the radiographic findings are doubtful in infants, the diagnosis should be available from the history and clinical response to conservative therapy. In a previous report we stated that the transition area from the aganglionic segment to the normally innervated bowel above it was difficult to recognize at operation. With increased experience, we find that even when the bowel has been well decompressed, the transition zone is usually quite easy to identify in the gross. Though there may be very little difference in the size of the segments, the hypertrophied bowel above the obstruction feels thick when rolled between the fingers, while the achalasic segment feels normal. Thus, although accurate preoperative diagnosis should obviate exploration for obstruction of undetermined origin, the diagnosis can usually be made at the operating table if it has not previously been established.

The following is an example of an early case in which the megacolon had not developed far enough to permit easy radiographic diagnosis.

CASE 1 (Children's Hospital No. 74584).—H. T., an infant, the youngest of four children, was born at full term by spontaneous delivery with a birth weight of 8¼ pounds. His three siblings are normal. He refused feedings on the first day of life, and severe abdominal distention developed very rapidly. At the age of 4 days he underwent exploratory laparotomy for intestinal obstruction, in the hospital where he was born, but the findings were not immediately available. According to the mother, he was discharged after twenty-five days, but readmitted a few days later for further enemas, remaining in the hospital ten days. Immediately after discharge he became constipated and distended and the mother administered two enemas a day thereafter. In spite of this he continued to vomit almost every day and the abdominal distention remained chronic. He was admitted to the Children's Hospital Sept. 18, 1950, at the age of 5 months, with acute intestinal obstruction. Examination showed marked abdominal distention (Fig. 1), palpable fecal masses, and dilated intestinal loops, dehydration, toxicity, malnutrition and retarded growth. He had a rather severe hypochromic (nutritional) anemia.

Because no information was immediately available about the original laparotomy, the possibility of secondary adhesions could not be excluded, although the diagnosis of aganglionic megacolon was strongly suspected. For this reason conservative treatment was elected. The baby responded well to high enemas, with complete recession of the abdominal distention, vomiting, and all obstructive symptoms. The initial barium contrast studies were equivocal.

On Oct. 10, 1950, three weeks after admission, a report was received about the neonatal exploratory laparotomy. This report stated that, "The small bowel and proximal

half of the large bowel were markedly dilated.'' The sigmoid was adherent to the right side of the abdomen but not obstructed there. A rectal tube was passed into the sigmoid and the bowel was completely deflated through this tube. ''It was noted that there was some stricture of the bowel in the rectum and this was dilated. . . . This baby has a large and redundant sigmoid colon. . . .'' This information confirmed our diagnosis of true Hirschsprung's disease. On the same day, a repeat barium study demonstrated the lesion radiographically (Fig. 2, *A* and *B*).

Fig. 1 (Case 1).—Flat film of the abdomen during one of the patient's episodes of acute obstruction. The fecal masses in the distended colon are visible.

With the diagnosis established, the question of optimal time for operation arose. The patient's general condition was still not good. Since with good supervision and properly given enemas these patients may be maintained in good health for a long time, it was decided to defer operation until he was a little older and in better condition. The infant was discharged Oct. 17, 1950, with detailed instructions to the family regarding daily enemas, mild laxatives, and frequent visits to the outpatient department for supervision. However, they lived 150 miles away and were unable to keep the clinic appointments.

The baby was admitted to Children's Hospital the second time, Dec. 3, 1950, again in acute obstruction. The mother had made a conscientious effort to keep the baby's bowel open with enemas and had succeeded to the extent that the general condition was markedly improved, the nutritional state much better, and the blood picture normal, although she had not been able to prevent obstruction entirely. The obstruction again responded promptly to gastric suction and a series of high enemas in the hospital. In view of the difficulty of providing adequate supervision and the danger of recurrent and possibly fatal acute obstruction, and in view of the child's greatly improved general condition, it was

decided that operation should be performed. Two weeks were required for preoperative preparation and surgery was deferred an additional week because of an upper respiratory infection.

On Dec. 26, 1950, Swenson's operation was done, resecting the achalasic terminal segment and enough of the dilated bowel to provide compatibility in size for the para-anal anastomosis. The child had the first spontaneous bowel movement on the second post-

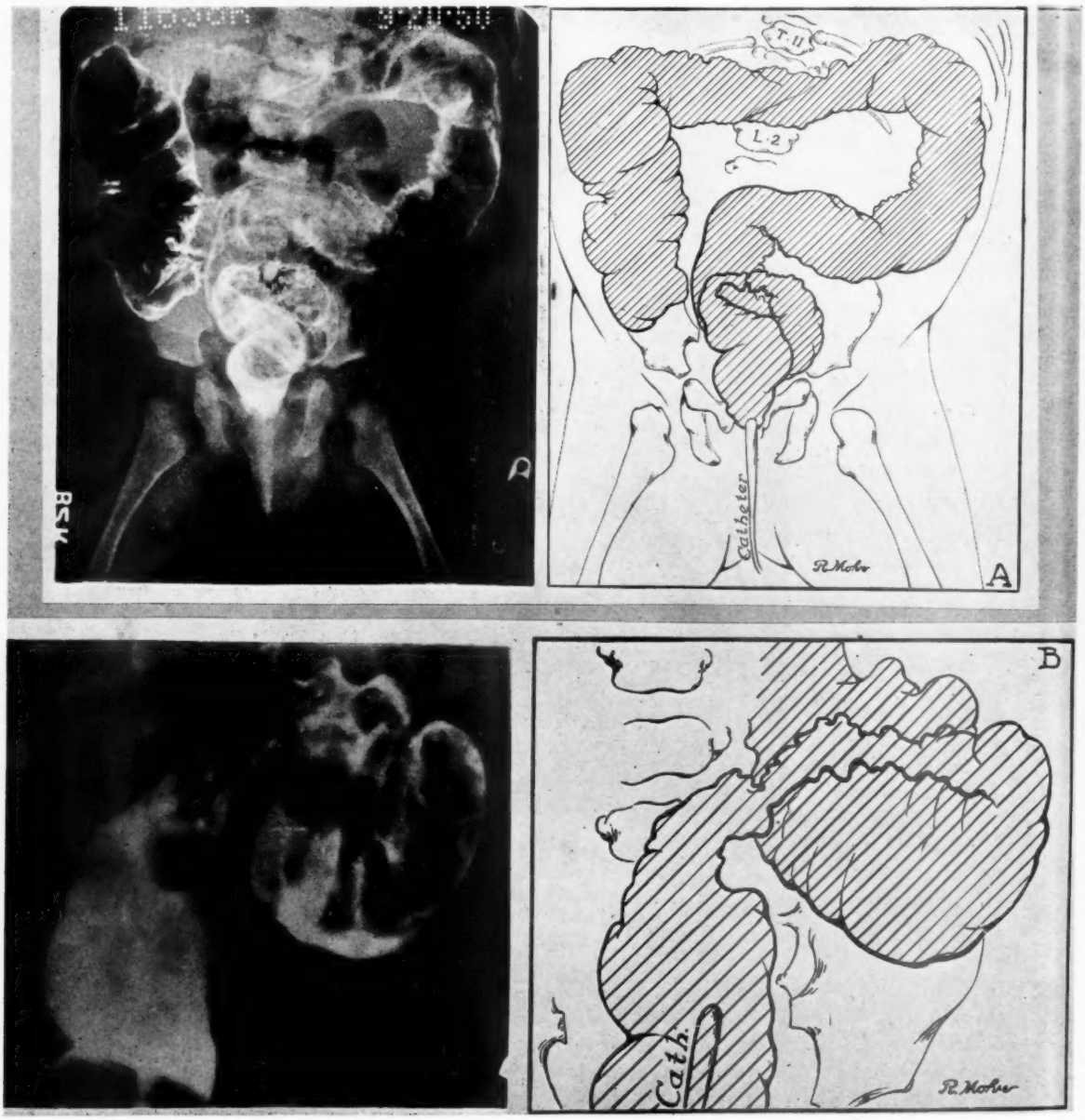

Fig. 2 (Case 1).—*A*, Postevacuation film after barium enema at the time of first admission. The megacolon is not pronounced because of the extreme youth of the patient and evacuation of the bowel by enemas before the film was made. The tracing shows the upper limit of the achalasic segment but the contrast between this and the dilated bowel is not marked. The films were interpreted as equivocal. *B*, One of a series of spot films made during barium enemas on Oct. 10, 1950. The narrowed segment was consistently present in all spot films and under the fluoroscope. This was interpreted as confirmatory evidence of aganglionic megacolon. The similarity of contour in the two sets of films made three weeks apart is quite striking.

operative day and recovery was entirely uneventful. He was ready for discharge by the sixteenth postoperative day, but because of the difficulty of follow-up, he was kept in the hospital until after the four-week postoperative barium enema. This was done Jan. 23, 1951 (Fig. 3, *A* and 3, *B*). He was discharged Jan. 25, 1951, having regular spontaneous bowel movements every day. There was no disturbance of bladder or rectal control.

The resected terminal segment showed a complete absence of ganglion cells in both Auerbach's (myenteric) and Meissner's (submucous) plexuses, while the ganglia were normal in the hypertrophied segment that had been removed with it.

Fig. 3 (Case 1).—*A*, Barium enema four weeks after operation (Jan. 23, 1951). The normal size and contour of the colon are demonstrated. *B*, Flat film taken the day following the barium enema shown in 3*A*. The complete spontaneous evacuation of the barium is seen. The improved condition of the patient may be emphasized by comparing this film with the preoperative flat film shown in Fig. 1.

Comment.—In this case the diagnosis was clouded by lack of information regarding the findings at the original laparotomy. Although we strongly suspected the proper diagnosis, assurance was lacking because adhesions from the previous operation might have produced the existing incomplete obstruction. The history of early onset and the response to enemas and laxatives would otherwise have made the diagnosis fairly certain without definitive radiologic proof. When available, as it uniformly is in the more advanced case, radiographic demonstration of the lesion offers highly desirable confirmation.

Most of our experience has been with young children, but the following case illustrates the pattern of the disease in an adult.

CASE 2 (Cincinnati General Hospital No. 269156).—W. C., a 25-year-old white man, gave a history of severe bowel difficulty from birth. Within a day or two after birth he had become distended and vomited and the parents were told that he had a "paralyzed bowel." One to three enemas were required daily, administered by the mother, until the age of 9 years. At this time he was taken to a specialist, who did a sigmoidoscopic examination under spinal anesthesia, and after barium studies the parents were told that the patient had Hirschsprung's disease. No operation was advised. For a short time thereafter the patient improved and had spontaneous bowel movements. Then the trouble recurred and the enemas were resumed. Finally he stopped school in the ninth grade because, even with the enemas, he had frequently recurring abdominal distention, cramps, and obstipation. He found that if he took one day off a week and devoted it to a series of high colonic flushes, he could get along quite well.

Five weeks before admission to the Cincinnati General Hospital, he obtained work which prevented him from taking a day off each week for bowel cleansing. He was admitted to the hospital on Nov. 7, 1950, with an "acute surgical abdomen." Exploration revealed a perforation of the sigmoid with generalized peritonitis. The entire left colon was hugely dilated and hypertrophied with similar but less pronounced changes all the way to the ileocecal valve. In the sigmoid there was an abrupt transition to a normal-looking, narrow terminal segment. The perforated sigmoid was exteriorized as a tangential colostomy and a cecostomy was done. With intensive supportive and antibiotic therapy, the patient recovered from the generalized peritonitis. His general condition improved slowly, and meanwhile a barium contrast study showed the typical pattern of aganglionic megacolon with the dilatation ending in the sigmoid and a normal-looking terminal segment. The operative findings were thus confirmed.

On Jan. 4, 1951, Swenson's operation was performed. In the two months since enterostomy, the dilatation of the proximal colon had receded, though the lower half of the left colon remained hugely dilated and hypertrophied. Resection of this area (including the tangential colostomy) together with the achalasic terminal segment was done and a pull-through para-anal anastomosis with the proximal descending colon was made.

The postoperative course was satisfactory. Spontaneous bowel movement was delayed because of the cecostomy but occurred on the tenth postoperative day. On the sixteenth postoperative day, sigmoidoscopic examination showed the anastomosis to be healed without stricture and the bowel above to be normal. The cecostomy began to close spontaneously, but because the patient was anxious to leave the hospital and return to work, it was surgically closed on Jan. 24, 1951.

The specimen (Fig. 4) showed the resected bowel, except the terminal three to four inches of the achalasic portion, which was separately removed under Swenson's technique. Both portions of the achalasic segment showed a complete absence of parasympathetic ganglion cells in both the myenteric and submucous plexuses, while the ganglia were normal in the hypertrophied bowel above.

The patient was discharged Feb. 7, 1951, having normal spontaneous bowel movements daily. There was no impairment of vesical or rectal control and the urge to defecate was normal. There was no impairment of sexual potency.

Comment.—We believe that it is comparatively unusual for patients with true Hirschsprung's disease to survive untreated to adult life. Since differential diagnosis has been available only in the past three to four years, most of the reported cases of megacolon in adults do not provide enough information to distinguish one type of "idiopathic" megacolon from another. Most of the proved cases reported in detail with microscopic findings have been autopsy cases. Where the patient has survived, it has always been with the help

of a colostomy or by laborious and incessant use of enemas. It is true that some cases have been temporarily benefited by sympathectomy and prolonged medical management, but we suspect (in agreement with Bodian, Stephens, and Ward[2]) that the preoperative preparation with enemas and the postoperative medical management with enemas and related measures are responsible for the improvement. We further suspect that those patients in whom permanent benefit has been achieved by intra-abdominal segmental resection and medical

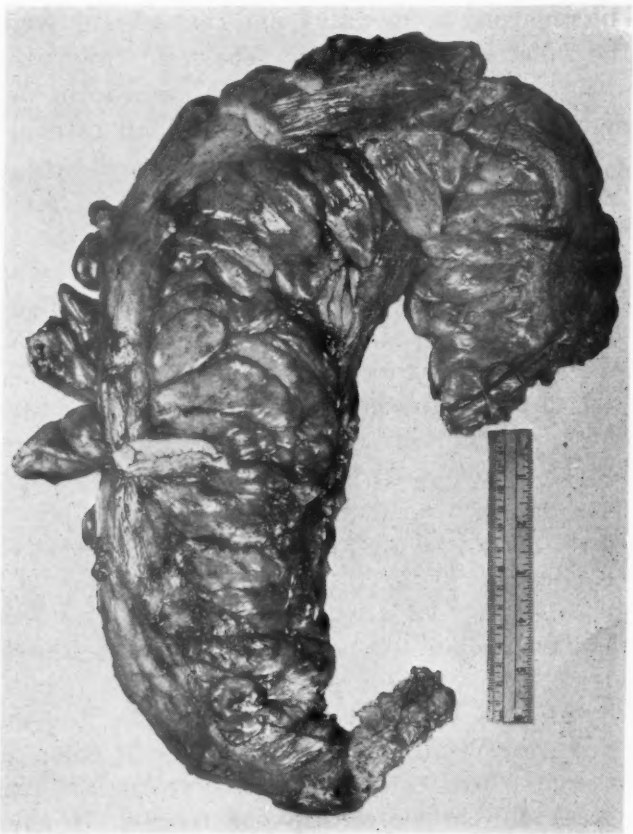

Fig. 4 (Case 2).—Photograph of part of the specimen removed. The lip of skin from around the tangential colostomy is visible in the lower mid-portion of the specimen. The transition from the dilated and hypertrophied bowel to the narrow achalasic segment is clearly seen. Only the proximal four inches of the achalasic segment is shown here. The distal three to four inches was separately removed as part of the pull-through technique of Swenson.

management actually belong in the category of functional megacolon and do not have true Hirschsprung's disease. If they have true Hirschsprung's disease, they have not been followed long enough to develop recurrence of the trouble. Resection of a long segment of bowel not only clears the existing impaction but renders the feces more liquid and delays the formation of a new impaction. But sooner or later, depending upon how much colon was resected, water absorption in the bowel becomes adjusted, a new impaction develops, and the disease recurs. There are many reports of recurrence, albeit long delayed, after total colectomy with anastomosis of ileum to the supposedly nor-

mal rectal stump at the level of the peritoneal reflection. Upon consideration, it becomes apparent that while either sympathectomy or intra-abdominal segmental resection may produce transitory improvement, for the reasons given, permanent cure can be achieved *only by removing the obstructing achalasic segment.*

2. Functional Megacolon.—In our previous paper,[15] the term "idiopathic" was retained for this type of megacolon. We now believe that no case of megacolon need be regarded as idiopathic and that a better term for this group of cases would be functional megacolon. The term "idiopathic" has led not only to confused interpretation but has, as the cases to be described demonstrate, led to an unfortunate tendency to regard all cases of megacolon as idiopathic, with the consequent misapplication of treatment. In this group of cases the source of the obstruction is, we believe, the *fecal impaction* itself, which derives from one or more of several factors. Frequently a spastic anal sphincter is present, but whether it is a cause or result of the impaction is uncertain, and this is not clinically important. Usually faulty bowel care and training is the source of the difficulty and may often be traced back to infancy. The onset, however, is *never at birth,* in sharp contrast to the first group of cases described. Every pediatrician knows that an improper formula or, as the child grows older, an improper diet, may produce a severely constipated stool. If the passage of this stool is painful and if the diet is not corrected, the child is less and less inclined to go to stool and the impaction grows steadily worse. A fissure may develop, or there may be simple reflex anal spasm from painful defecation, but either of these is only incidental to the obstructing fecal impaction. At any rate, the "fear of the pot" has been mentioned by many writers, and this cycle of events is by far the commonest basis for functional megacolon. There is a small group of cases in which diet and training are not necessarily at fault. As we pointed out in 1950,[15] an occasional patient is seen in whom a congenitally long and redundant colon (dolichocolon of Martinotti) is present. This excessive absorptive surface removes too much water from the feces and chronic constipation results. It may not become apparent until the child is old enough to progress from the soft stool of infancy to the formed stool of childhood and adult life. Even then megacolon may not develop because in this laxative-and-enema conscious country, few people without organic disease are permitted to remain constipated if they own a radio. The first recognized indication of the presence of dolichocolon may be volvulus of the sigmoid in adult life, but in the rare individual it may be a factor in the development of megacolon. Jones and Morton[13] reported good results from resection of the redundant bowel more than twenty years ago. Since elongation of the bowel is much more often the result of constipation and obstructive impaction than the cause of it, very few cases require surgery. The following is a typical example of functional megacolon.

CASE 3 (Children's Hospital No. 7129).—C. M., a 15-year-old white boy, was first seen on March 25, 1950. According to the mother, he was born at term with low forceps delivery, and weighed eight pounds at birth. There were no bowel symptoms of any kind

during the first year of life. At the age of 12 months the child began to show evidence of chronic constipation which was treated with daily administration of prune juice, and enemas every two to three weeks. He improved considerably and got along well until the age of 6 when he started school. Severe constipation returned and did not respond to the simple methods previously employed. Intervals of seven to ten days during which he had no bowel movements were followed by periods of five to six days during which there were abdominal cramps, fecal incontinence, and multiple small loose stools.

He was seen by several physicians who advised the parents that there was "nothing the matter with him" although one physician advised appendectomy. This was refused for lack of funds. The incontinence was attributed to willfulness by the boy's father and his teachers and he was severely and repeatedly punished both at home and at school. In spite of this handicap and that of repeated bouts of abdominal cramps, he did reasonably well in school and was in the ninth grade when first seen.

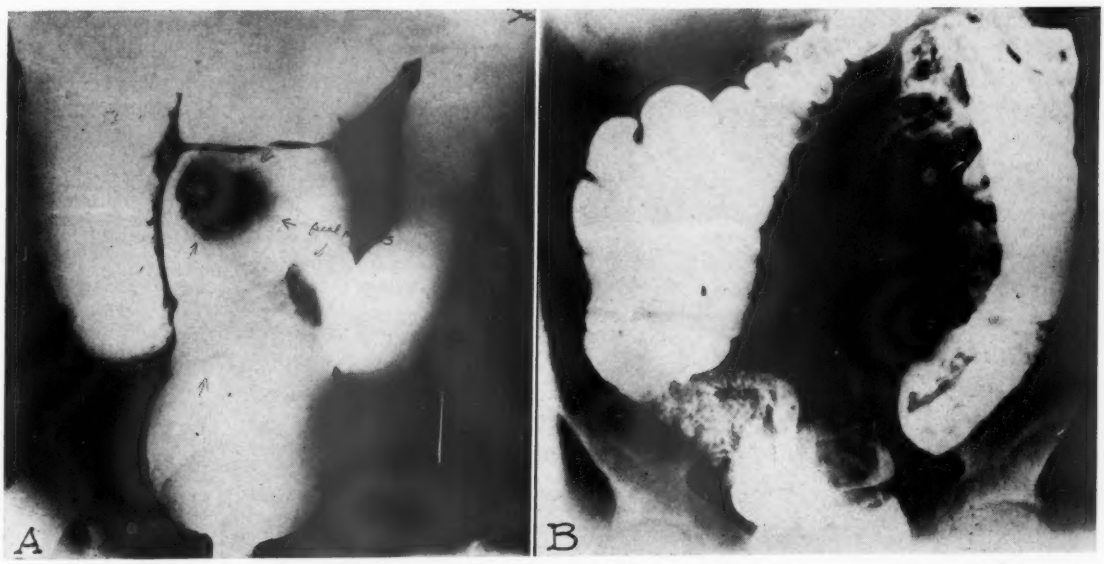

Fig. 5 (Case 3).—*A*, Anteroposterior projection of the barium enema in the filling phase. The dilatation extends all the way to the anus and there is marked elongation of the colon. *B*, Evacuation film during the same examination, showing very poor emptying and the persistent elongation of the colon.

On examination, the boy was slender but well developed and adequately nourished. There was no abdominal distention and the musculature was good, but fecal masses were readily palpable. Rectal examination showed a normal sphincter without spasm and a huge fecal impaction in a widely dilated rectal ampulla. Barium enema showed a massive megacolon extending all the way to the anal canal (Fig. 5, *A* and *B*) and proximally to the cecum. Emptying was very inadequate. The sigmoid was markedly elongated and coiled on itself, but dilated throughout.

The patient was admitted to Children's Hospital March 28, 1950, and started on medical treatment as described later in the text. Within one week, he was having spontaneous bowel movements and was discharged from the hospital April 7, 1950, after ten days in the hospital. Both the patient and his mother were given detailed instructions for following the regimen started in the hospital. He has been entirely well since then. His bowels move normally and spontaneously once and sometimes twice a day. There has been no incontinence since he left the hospital. Barium contrast studies show complete evacuation and normal contour and shortening of the elongated colon, but tone has not completely returned to normal, as indicated by the filling film (Fig. 6, *A* and *B*).

Comment.—This was a case of "idiopathic" megacolon in which digital examination failed to demonstrate any obvious source of obstruction. What distinguished it from other cases? The onset was late, *not at birth.* Radiographic studies demonstrate that the dilatation of the colon extended all the way to the anal canal. Digital examination showed a normal anus. The reasonable conclusion was that the cause of the obstruction was the fecal impaction itself. When this was corrected by medical means, the patient was cured. If, after a thorough trial of medical management conscientiously followed, the patient is still constipated and still displays an elongated colon on radiographic examination, then, and only then, should surgical intervention be considered and intra-abdominal resection of the redundant colon with end-to-end anastomosis might be indicated. Irreducible or recurrent volvulus of the sigmoid also constitutes an indication for surgery but the operation is done for dolichocolon rather than megacolon.

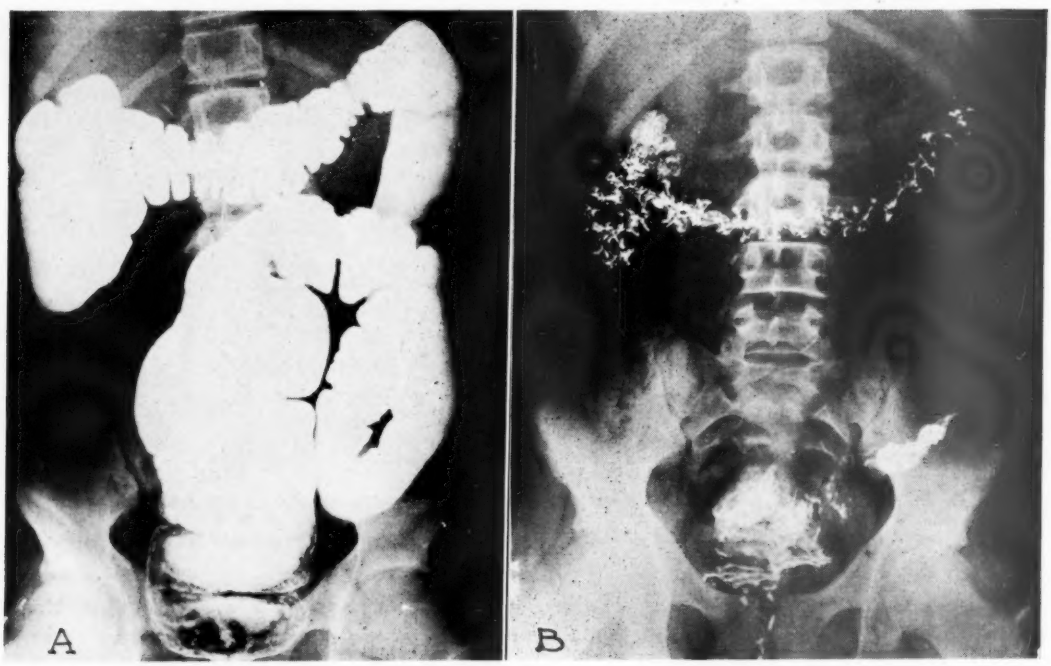

Fig. 6 (Case 3).—Barium contrast after one month of treatment. *A*, Represents the filling phase showing that completely normal tone has not been restored and that the bowel is still distensible into the configuration of megacolon. *B*, Shows the postevacuation film. The normal emptying is clearly seen and the patient was clinically well at this time. It is apparent, however, that without careful follow-up and continued bowel training the condition might readily recur.

It is this group of cases that has contributed so much to the megacolon problem. This group alone could benefit permanently from intra-abdominal segmental resection of the bowel although such a procedure is unnecessary in most cases. The rectum and lower sigmoid are intrinsically normal and when part of the bowel is resected, softer stool is delivered to the anus, no intrinsic obstruction is present, and the patient is cured. As indicated in the discussion of Case 2, it is probable that the preoperative preparation alone, involving

cleansing enemas and laxatives, if followed by proper bowel training, would have effected a cure. The same may be said of patients permanently cured by sympathectomy and medical management. It is impossible to classify the reported cases positively because of insufficient data to permit a conclusive differential diagnosis, but the pattern of results is so striking that the validity of this conclusion is almost inescapable. In all of the cases reported from the Great Ormand Street Hospital, where a proper differential diagnosis was made, medical management alone sufficed to effect a cure. The same has been true in all of our own cases where the obstruction was due to impaction alone, without congenital dolichocolon. It cannot be emphasized too strongly that congenital dolichocolon is extremely rare and that the vast majority of cases of functional megacolon do not require surgery of any kind. It is perhaps unwise to include within the category of functional megacolon the cases in which dolichocolon is a factor. Dolichocolon is seen more commonly without secondary megacolon and presents itself as recurrent volvulus in patients who have been chronically constipated and habitual enema-and-laxative takers all their lives. When megacolon does arise with dolichocolon, as it may rarely do, it is a functional result of that condition, and the bowel itself is intrinsically normal. For this reason it is included here.

3. Symptomatic or Organic Megacolon.—Organic megacolon has long been recognized and separated from the "idiopathic" cases, and yet it is distressing to note how often the diagnosis is missed because of the widespread impression that all megacolon is "idiopathic." The cause of the obstruction is grossly demonstrable, usually by simple digital examination. The commonest single cause in children is stricture following operations for imperforate anus. Failure to provide adequate dilatation over a long enough period of time permits progressive cicatricial narrowing of the surgically produced anal opening. Bowel movements become increasingly difficult and painful, and as fecal impaction develops and persists, the situation grows worse and an extensive megacolon may result. Other causes of obstruction may be tumors, intrinsic or extrinsic, and, though the anomaly is rare, the congenital stricture of Type I anorectal anomaly (classification of Ladd and Gross). Usually the symptoms do not develop rapidly. They represent a compounding of such elements as the progress of the stricture or tumor with the transition from soft to formed stools in late infancy. The following is an example of this situation.

CASE 4 (Children's Hospital No. 72251).—K. C., a 7½-year-old white boy, was first seen April 15, 1950. According to the mother his delivery was at term, and uncomplicated, but she noticed as soon as she took him home that he had to "strain a good deal" to move his bowels. By the time he was 4 months old he had severe and intractible constipation and abdominal distention. However, he took his feedings well and did not vomit. The mother consulted her attending obstetrician and was told that the infant had had a "closed rectum" requiring a "small operation to correct it" (presumably a Type II imperforate anus), and that he would "outgrow" the symptoms.

From the age of 4 months, the child was severely constipated. The mother gave him enemas with a small tube and frequent doses of citrate of magnesia, and was able to produce bowel movements at irregular intervals. The child would go as long as three weeks without a bowel movement and abdominal distention increased. He would cry in pain and

when this situation grew severe the mother would give an enema. In spite of all this there was no vomiting until the child was 4 years of age. From this time he had recurrent episodes of distention, cramps, and vomiting, usually after a period of complete constipation lasting two to three weeks. This would be followed by a week of complete incontinence with multiple small stools which were obviously painful. Since several doctors had told the mother (without doing rectal examinations) that there was nothing wrong with the child, she and his father (as in Case 3) attributed the incontinence to willfulness. He was punished both at home and at school for soiling his clothes, yet the mother's description of his efforts to avoid going to stool were pitiful to hear. He would cry, vomit and "squinch himself together," shifting from one foot to the other, but in spite of all efforts would soil himself several times a day. He failed the first grade because he had to be kept home so much during the attacks of vomiting, cramps, and fecal soiling.

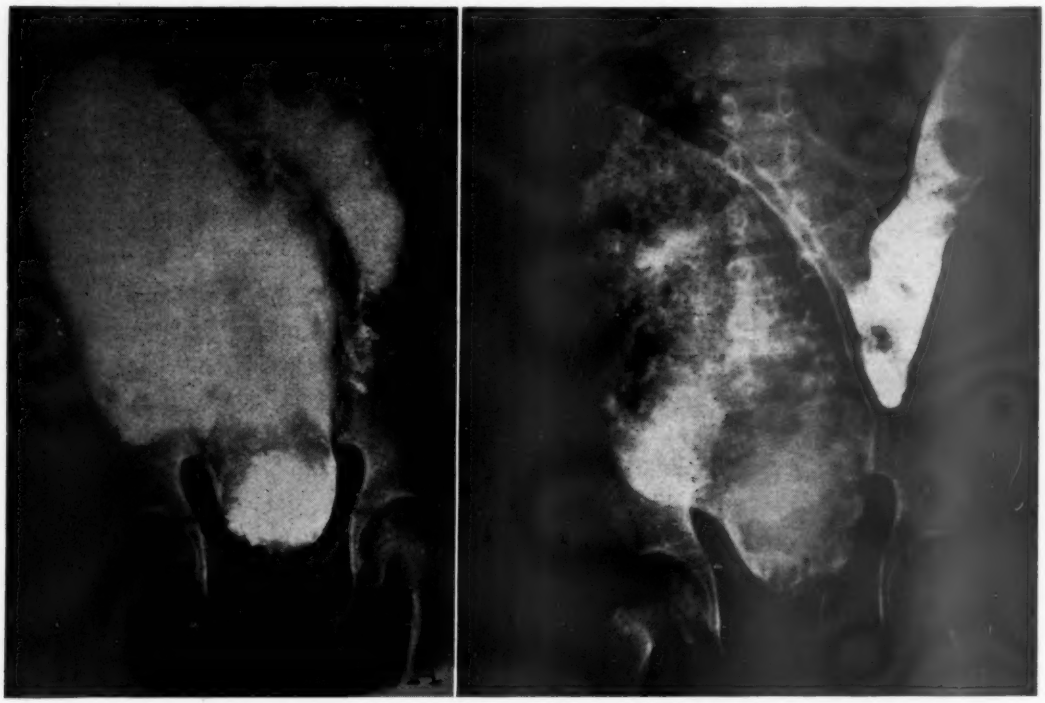

Fig. 7 (Case 4).—*A*, Shows the filling phase of the barium enema with a massive megacolon in which the dilatation extends all the way to the anus. Note that with the elongation incident to obstructive dilatation and hypertrophy the sigmoid lies in the right side of the abdomen. *B*, Shows the postevacuation film of the same examination. The child was entirely unable to empty the colon and large residual fecal masses are seen.

Examination showed a vigorous, alert little boy of 7, somewhat small for his age but well developed and nourished. The abdomen was markedly distended and fecal masses were palpable. The costal margins were flared, producing a conical "barrel chest." (The child took pride in this, saying that his chest was "like Tarzan's.")

There was gross soiling of the perineum and underclothes though these were clean when the child left home. The anus was so narrow that not even the little finger could be introduced, the aperture being estimated as about 0.5 cm. in diameter. For this reason the rectal ampulla could not be palpated.

The patient was admitted to Children's Hospital, April 17, 1950. Barium enema showed a massive megacolon extending all the way to the anus (Fig. 7, *A* and *B*). Initial anal dilatations were done with urethral sounds and later with Hegar cervical dilators under general anesthesia. The stricture was so tough and resistant that for a time a plastic

procedure was seriously considered, but by repeated and persistent dilatations it became possible to insert a dilating finger without anesthesia. Meanwhile, medical treatment with enemas and laxatives was begun and meticulously followed. The child was discharged May 15, after twenty-eight days in the hospital because he contracted mumps, and was re-admitted May 31 for an additional twenty-four days.

Since the second discharge, June 24, 1950, he has followed conscientiously the regimen laid down in the hospital. Daily digital dilatations were done at home by the parents. The bowel training program has been followed. There has been no fecal incontinence at any time and bowel movements are regular and spontaneous. He comes regularly to the outpatient department for supervision and further dilatation with Young hard rubber dilators. Barium enema shows normal emptying and shortening of the elongated sigmoid (Fig. 8, *A* and *B*). The abdominal distention has disappeared and the thoracic contour is returning to normal. The boy is doing well in school.

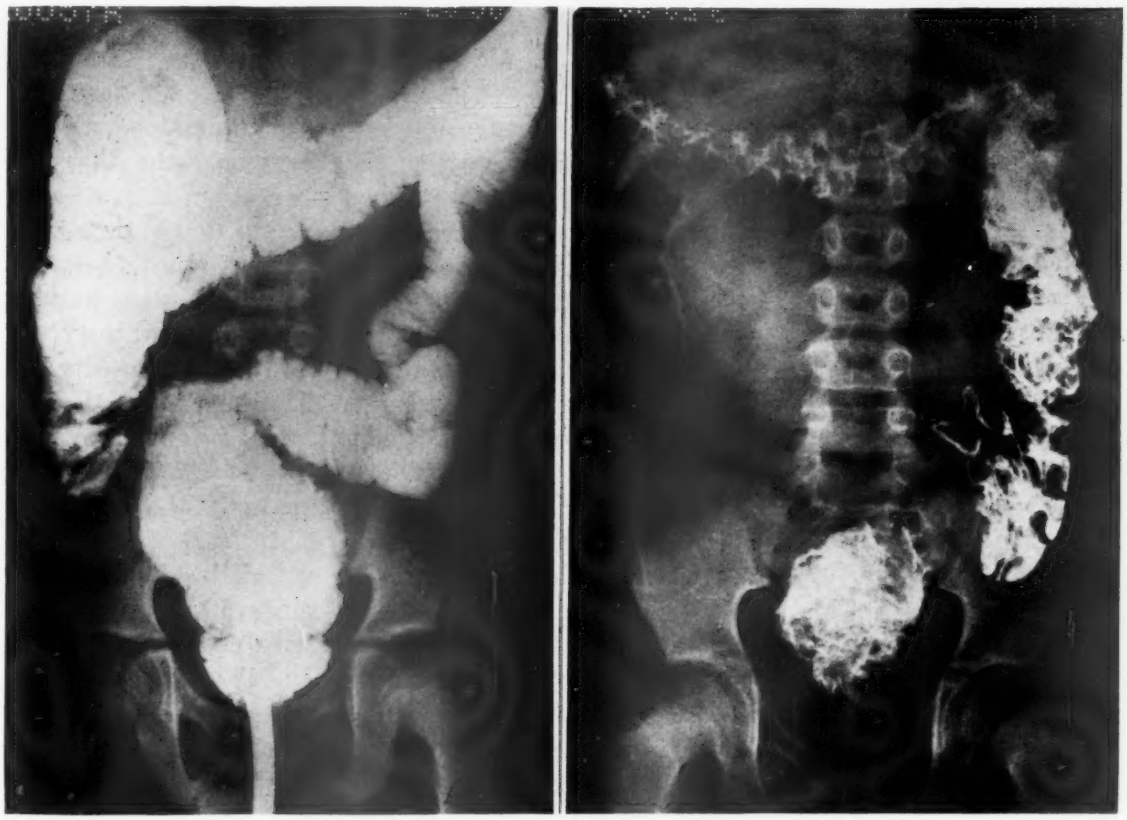

Fig. 8 (Case 4).—Barium contrast study, twenty-one weeks after initiation of treatment. *A*, The filling film. There has been a marked recession of the megacolon with both shortening and contraction of the dilated and hypertrophied bowel. Normal tone is not fully restored since the bowel can still be distended beyond normal proportions. *B*, The post evacuation film shows effective emptying and greatly improved tone. The general configuration is approaching normal and the child is clinically well. It is evident here also, however, that unless conscientious supervision is continued, the condition might readily recur.

Comment.—The diagnosis here is obvious, either to the clinician or to the radiologist. If the clinician has failed to do a digital examination of the anal canal, the radiologist, noting that the dilatation extends all the way to the anus, can reasonably say that unless the onset of symptoms was at birth, the case is not one of true Hirschsprung's disease and can suggest further clinical examination. If no gross organic obstruction is found, the case is one of

functional megacolon; if tumor or stricture is present, the examining finger finds it. Thus, in children, there should seldom be any difficulty about the diagnosis. A real congenital stenosis low in the colon might seriously confuse the picture. Fortunately this is an extremely rare anomaly, though when present in sufficient degree to produce megacolon, it might be difficult to distinguish clinically or radiologically from true Hirschsprung's disease. Nevertheless, abdominal operation is essential in either situation, and here the differential diagnosis might not be made until the microscopic sections had been studied. A cure would be effected and there would be nothing "idiopathic" about the end result. In other patients, where a high tumor produces the dilatation and hypertrophy, late onset alone is enough to distinguish the case from aganglionic megacolon.

MANAGEMENT OF MEGACOLON

Once the pathologic physiology of megacolon is clearly understood, the appropriate treatment becomes apparent. Although therapy of the three major types has been referred to briefly in the foregoing section, it can be further clarified by more specific discussion. Before presenting this in detail, however, special emphasis should be given to the importance of Hiatt's[10] observations on the use of enemas in megacolon. Everyone who has dealt to any great extent with this condition has seen cases in which a sudden and unexplained fatal collapse has occurred when the patient appeared, temporarily, to be getting along well on conservative management. Hiatt has shown that the use of tap water for enemas may result in a sudden "water intoxication." There is a sharp drop in the plasma sodium, chloride, and proteins, and in the serum potassium, and a rise in the plasma volume. Apparently the hypertrophied and dilated bowel absorbs water much more rapidly than does the normal colon and the disturbance of electrolyte balance, especially of sodium, may be fatal. This danger is common to all types of megacolon and it is obvious that tap water should not be used for decompressive enemas. Hiatt has pointed out that isotonic saline can safely be used in all such patients except those with impaired cardiac or renal reserve. In these cases he recommends the use of a 7 per cent gelatin solution. With this important precaution constantly in mind the management of the three major types of megacolon may be summarized.

1. Treatment of Achalasic or Aganglionic Megacolon (True Hirschsprung's Disease).—As indicated earlier, we do not believe that either sympathectomy or intra-abdominal segmental resection exerts any direct or permanent beneficial effect on true Hirschsprung's disease. The only rational treatment is removal of the obstructing segment. Swenson's operation (or Hiatt's modification of it) appears to offer an entirely satisfactory method of effecting this correction. The operation produces no impairment of anal sphincter control or of bladder function. It is essential, of course, that the pelvic dissection be conducted directly against the fascia propria of the rectum to avoid injury to the pelvic nerve plexuses, since this injury might result in sexual impotence.

While most of our experience has been in children, none of whom is yet old enough for evaluation of this possible complication, we have reason to believe that potency is not impaired. In the case of the 25-year-old man (Case 2), there was no impairment of sexual potency. We have had occasion to dissect out the rectum in the same manner, with ileostomy instead of a pull-through procedure, in total colectomy for ulcerative colitis in young adult men, and in none of these has there been any impairment of sexual potency.

Where only a part of the colon is dilated and hypertrophied, and when it is possible to obtain a segment of a size readily compatible with para-anal anastomosis, we prefer the one-stage procedure which Swenson has described. The hospitalization is short and convalescence rapid. In some patients, such as those who not only have acute obstruction but in whom the impaction cannot be relieved and the bowel decompressed and cleared by enemas, a preliminary colostomy may be necessary, as described by Stephens.[2] If there is enough movable descending colon of reasonably normal caliber to permit para-anal anastomosis, we do not wait for the distended bowel to return to normal, but proceed with Swenson's operation as soon as the patient's condition permits. If so much of the colon is involved in the process of dilatation and hypertrophy that needless sacrifice of too much potentially normal bowel would be involved, we prefer to do a colostomy and wait until the dilatation and hypertrophy have receded enough to be compatible in size with the para-anal terminal rectum. The pull-through procedure can then be done without sacrificing any bowel but the achalasic segment. The interval before the dilated bowel returns to a usable caliber depends, of course, on the duration of the disease and the effectiveness of home decompression with enemas before the patient consults the physician. It is logical that the older the patient and the less conscientious he has been with enemas and laxatives, the greater will be the dilatation and hypertrophy and the amount of colon involved in the process. By the same token, the greatest hypertrophy and dilatation will be in the portion of the bowel just above the obstructing achalasic segment, and this will be the last to return to normal. In the adult patient described (Case 2), the entire colon was affected, but after the mandatory colostomy, all but the lower third of the descending colon returned to a usable caliber within six weeks. Rather than prolong his disability for several more months, as would have been required for this thickened and dilated bowel to return to normal, operation was done as soon as there was a long enough segment of normal bowel to permit it, and the remainder sacrificed.

In estimating the length of available normal bowel by contrast radiographic studies, it must be remembered that much of the elongation is due to obstructive hypertrophy and that after operation the bowel will shorten. If the pull-through results in a tightly stretched descending colon, subsequent shortening could produce a sharp angulation at the first fixed point, such as the splenic flexure. Therefore, it is necessary to make certain that enough descending colon is preserved to permit its implantation in the pelvis with plenty of slack in the intra-abdominal portion.

With these precautions in mind, Swenson's operation has, in our experience, been clinically and physiologically satisfactory. It is a fairly formidable procedure, but the risk is justified by the results, provided proper differential diagnosis is made and the procedure is reserved only for cases of achalasic megacolon.

2. Treatment of Functional Megacolon.—As mentioned, the obstruction in cases of functional megacolon is due entirely to the fecal impaction, and except in the rare cases where dolichocolon is a factor, surgery is never needed. The initial treatment consists of removal of the impaction, usually with a combination of digital excavation and multiple enemas. Where severe sphincter spasm with or without fissure is present, general anesthesia may be necessary. Once the impaction is removed, daily enemas are required. These must be administered at the same time every day. Concurrently, the patient is started on nightly doses of a bland laxative. In our hands a proprietary preparation compounded from mineral oil, agar, and cascara has been found to be very satisfactory. As soon as the patient becomes convinced that he can have bowel movements without discomfort, the enemas are discontinued but the laxative is continued. Both in the hospital and at home the importance of a regular time for going to stool is stressed. In order to focus the interest and attention of these patients on this, a sort of ritual is set up. The laxative is taken at bedtime. The patient must get up in the morning in time to attend to his bowels before going to school or work. Immediately on arising he drinks a full glass of water. At breakfast, he drinks a hot liquid such as postum, cocoa, coffee, or even water. Immediately after breakfast he goes to the toilet. If he fails to have a spontaneous evacuation another dose of laxative is taken and the ritual is repeated at supper time. If no spontaneous bowel movement occurs after supper, an enema is given. The importance of proper diet is stressed and the patient is required to have fresh fruit or a fresh vegetable with each meal. Constipating foods are avoided or intake is limited. Adequate intake of water throughout the day is insisted upon.

On this regimen* we have had little difficulty in establishing normal bowel habits within two to three weeks, even in very young children. Occasionally Mecholyl or Mecholyl Bromide is used as a supplemental medication but is seldom necessary except in patients who do not follow the ritual conscientiously. When Mecholyl or its bromide is used, a dose of 100 mg. once or twice a day is given to young children, and 200 mg., once or twice a day to older ones. If there is any tendency toward diarrhea, the dose is reduced.

3. Treatment of Symptomatic or Organic Megacolon.—Organic megacolon is the familiar type in which the source of the obstruction is grossly demonstrable. The treatment depends upon the nature of the obstruction. If, as is most common, it is stricture, then a course of dilatation combined with medical rehabilitation of bowel function is sufficient. Frequently the stricture is so narrow and firm that the initial dilatations must be done under general anesthesia. Thereafter, they may be done with the finger, without anesthesia, and usually a

*We are indebted to Dr. Katharine Dodd for suggestions regarding long-term medical management and bowel training in the chronically constipated child.

parent must be taught to do them daily at home. The child must be kept under observation at suitable intervals for several years, to make sure that the anal canal remains open and that he does not deviate from the regular course of bowel training and habit. It is our practice to pursue the dilatation beyond the size of the adult finger with Young's dilators until the size of the aperture is somewhat larger than is actually needed, because the tendency of scar tissue is to contract again. The interval between dilatations is slowly increased, and usually after two or three years they may safely be discontinued.

When the obstruction is due to tumor, either intrinsic or extrinsic, operation is, of course, essential, and in the rare case of stricture not amenable to dilatation, a plastic procedure may be required. It is impossible to overemphasize the need for adequate and continued follow-up examinations and treatment. Until regular bowel habits, with the dilating effect of regular formed stools, are well established, the danger of recurrence is great. Since it takes the chronically dilated and hypertrophied bowel several months (or more, depending on the degree of advancement of the process) to return to its normal caliber and muscular tone, the slightest constipation or impaction, however temporary, retards recovery and favors recurrence. The patient cannot be regarded as well and in no danger of recurrence until the caliber and expulsive power of the bowel has returned to normal. Often, when the patient is clinically well and a postevacuation contrast film shows normal configuration and emptying, the persistently impaired tone of the colon can still be demonstrated during the filling phase of the barium examination.

SUMMARY AND CONCLUSIONS

1. The pathogenesis of megacolon has been discussed and a classification into three major types, on an etiological basis, has been presented.

2. The differential diagnosis and management of megacolon in its several forms have been presented.

3. The term "idiopathic" as applied to megacolon should be abandoned. The word "idiopathic" has become so firmly attached to megacolon that there has been a widespread tendency to dismiss every case of megacolon as "idiopathic" without even looking for a possible cause. Our thesis is that *no case of megacolon is "idiopathic,"* and that the pathogenesis of every case can always be found if sought for. Effective definitive treatment is available for each case if a conscientious differential diagnosis is made.

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Surgical History

Conducted by John R. Paine, M.D.

THE BARBER-SURGEONS

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IN MOST barber shops during the time of my childhood, there was a cabinet containing rows of numerous gold-trimmed and initialed shaving mugs for the many patrons who shunned shaving themselves. Properly honing and stropping the old-time straight razor, let alone using it upon oneself, was a task of no mean dexterity and was willingly left to the barber. All the modern safety shaving gadgets bear witness to this fact.

One can easily realize why, in medieval times, the barber was a necessary and highly appreciated craftsman. He was in close contact with the common people and since he had a somewhat professional status plus a dexterity in the use of cutting instruments, his aid was naturally sought in surgical treatment.

The medical practitioners of the time looked down upon any surgical procedure, holding such to be below their dignity. The Church undoubtedly had a considerable part in forming this attitude. The Council of Tours (1163) forbade surgery for the clergy on the principle: "The Church abhoreth bloodshed." Later the Council of Nimes (1284) and that of Bayeux (1300) decreed: "Let no subdeacon, deacon or priest exercise any act of surgery which extendeth of the cautery or incision." It must be remembered that in many cases the institutions in which an education could be obtained were operated by the Church, and consequently affected by Church policy. Thus when the Medical School of the University of Paris, which was an ecclesiastic institution, was developed in the thirteenth century, its students were expected to have undergone an initial period of clerical training and, of course, surgical instruction was both inhibited and looked down upon in that institution.

The clergy of early church history wore beards and when, in 1092, the Pope ordered all henceforth to have shaven faces, it required many barbers to keep them so. The monks in the monasteries took in and trained young men to do the barbering for them. These men were also taught letting of blood by venesection, for it was an ecclesiastic law that each individual in the clergy must be bled regularly. The monastic barbers became known as "razor et minutor" ("barbers and phlebotomists").

The monks were not only the teachers of the people, but were the early practitioners of medicine and surgery. In their ministrations to the sick and injured the monks used the barbers as their assistants, taught them much, and gave them ample opportunity to acquire surgical knowledge and dexterity.

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Thus it was that when Pope Alexander III banned surgery for the clergy, and the then regular physicians refused to touch this work, the barbers, with great delight, entered the field.

There were in those times very few surgeons having a higher education. Those who had emanated from the medical practitioners who entered the field. One author states, "Their number could be counted upon the fingers." Gradually their number increased and they formed a company known as the Surgeons' Guild. They at no time appear to have been a numerous body. The best estimate from the records puts their number at about twelve, but never more than twenty. They looked down upon and ridiculed the barber-surgeons and made many attempts to supervise and control them, but without success. Although the barbers had no Greek and less Latin, they were numerous, approachable, and, to a certain extent, practically competent.

The practice of organizing into associations for mutual protection and profit is a widespread human trend. These groups in early times were called Guilds, and their growth and distribution extended all over Europe and far into Asia. The spirit of incorporation into these associations became universal among all classes of dwellers in cities before the end of the fifteenth century. The clergy, regular and secular, of all grades; the legal, medical, and teaching professions; the merchant, shopkeeper, and craftsman; the persecuted alien; all were entrenched behind the bulwark of professional associations. In the two thousand years of their existence, the Guilds had the whole municipal, industrial, and social life of the Middle Ages, excepting the industry of agriculture, moving within their circle. The interests of the townfolk, including every activity—public, municipal, social, private, and moral—centered in the Guilds. They were the Chambers of Commerce, the Friendly Societies, the Trade Unions, the Freemasonary, and, to a degree, the Joint Stock Companies of the times. It was the age when the merchant's home was in his warehouse, which also served as his factory or shop, when the apprentice, somewhat after the fashion of an adopted son, lived with his master for the seven years of his servitude, and when to attain Guild membership secured a recognized and honorable position in the land. No other conventional organizations existed for the purpose of lightening the burden following the hard toil of the working day. The warm lifeblood of the times circulated in the Guilds. Their members lived in the same quarter of the city or town, stood by each other's honor, sat together at the feast, shared the same purchase, marched side by side in the pageant, acted together in the play, and fought together in the part of the city walls committed to their care. The spirit of devotion and honor was as strong among them as among the knights of higher rank. Honesty and fair dealing were exceedingly dear to them, and they followed the bier of the departed and paid wax for the rest of his soul.

The Craft Guilds in England, including those of the barbers and the surgeons, were alike in their executive setup. They were usually presided over by one or more masters elected by the membership. This office was decidedly authoritative. There were a varying number of assistants who acted conjointly as an executive committee, one or more wardens who supervised the

membership and the Guild property, and usually one or more surveyors who acted as inspectors of members' shops to prevent the use of inferior materials and to detect and report any violations of Guild rules or state laws.

The Guilds had their own courts wherein delinquent members were brought to trial before the master as judge, and usually the assistants as a jury. The prevailing punishment was a fine, but imprisonment could be recommended to the civil authorities. Rescinding of membership, seldom prescribed, was a ruinous punishment in that it deprived a man of his livelihood, for no one could practice a craft or profession without membership in or permission from a Guild. For the mountebank or charlatan, some bizarre punishments were invented. One Roger Clark, having been found guilty of fraudulently treating a sick person by tying a blank parchment about her neck, and it having been found that he was "in no way a literate man," and that he was "altogether ignorant of physic or surgery," it was adjudged that "the same Roger Clark should be led through the middle of the city, with trumpets and pipes, he riding on a horse without a saddle, the said parchment and a whetstone, for his lies, being hung about his neck, an urinal also being hung before him, and another urinal on his back."

The Barbers' Guild and the Surgeons' Guild, like most others of the time, originally partook of a religious character. Men met together for religious observances, for attending funerals of deceased members and their wives, for bestowing charities, and for feasting once a year. To a semisocial and religious group the gradual addition of secular or trade functions took place so that at length the Guild not only made rules and regulations for the conduct of its own members, but with the consent of the civil authorities built an ironclad monopoly which led to its being critical and meddlesome in the affairs of others. Thus is came about that the Surgeons' Guild was in perpetual warfare with the Barbers' Guild. The former wanted exclusive determination of who, among the barbers, should be permitted to practice surgery. The barbers had the greater influence and won the battle. Sidney Young, in his book *Annals of the Barber-Surgeons,* puts the matter pointedly:

> Of the two fraternities, the Barbers by the regular and every day nature of their calling, as shavers and hair cutters, together with the practice of surgery by so many of them, were the most likely to become the more popular company; their fees would surely be on a lower scale than those of the more aristocratic surgeons, and their numbers, with their constant intercourse with the citizens in their capacity as barbers, enabled them easily to extend their connections as surgeons.
>
> In all their contentions with the Surgeons Guild, as far as we know, they held their own well, and thus it was that their place in the city, as a Livery Guild of at that time an ancient standing, their position as the professors of useful and scientific arts, their numbers and presumable affluence, all rendered it desirable that they should be placed upon the same footing as the better class of Guilds, by their acquisition of a Charter of Incorporation, which they accordingly obtained from the young King Edward IV in the first year of his reign (1462).

The Charter is a lengthy document and, though granted to barbers, devotes itself entirely to surgery. Evidently the practice of surgery being the more hazardous to the public, it needed more and closer regulation. This would

seem so from the preamble which recites how "through ignorance, negligence and stupidity" of various barbers and other practitioners of surgery, many of the King's lieges had "gone the way of all flesh." Then at the request of "our beloved, honest and free men of the said Mystery of Barbers," the King grants them to be one body perpetual, etc.

The Corporation was to have perpetual succession and a common seal, to hold lands of a certain value, to be able to plead and to be impleaded, to make bylaws, to have the scrutiny and correction of (apparently all) surgeons in the city and suburbs, as also the oversight of all instruments and medicines, etc., and to have the power of inflicting punishment, by fine or imprisonment, on offenders. None were to practice surgery until examined and approved by the masters and presented to the mayor, and authority was given to the freemen of the Company to be admitted into the freedom of the city.

With this rather large package of authority for the Barbers' Guild, it can be surmised that the Surgeons' Guild would fall to the position of a voiceless minority. Evidently that is exactly what took place, for little is recorded of their activities until July 21, 1493, when an agreement was entered into between the Barbers' Guild and the Surgeons' Guild wherein the two bodies, now on friendly terms, were to work together harmoniously for the betterment of both companies. The introduction to this document is quaint enough to bear reproduction:

"This present wrytyng endentyd of composicyons made the XXI th., day of July in the yere of owyer lord God MCCCCLXXXXIII and the VIII th., yere of the reyne of kyng harry the VII th., William Martyn then beying mayre of this cyte of london betwyxt the felishippis of surgeons enfrannches wt in the cyte of london on that on p'ty And the felishippis of barbours surgeons and surgeon barbours enfranchessid i the seyd cyte on the other parte witnesyth that the sayde felyshippys of their common assent and mere mocyons ben codescedyd and agreyd togethir the day and yere aboue sayd, in man and form folowyng:"

Then it goes on to say that no alien or foreigner shall be permitted to practice surgery without consent of the wardens, that the wardens are to have oversight of the membership, and to examine all candidates. Those found to qualify were to be sworn into membership. Any member having a seriously ill patient in danger of death was required to call the wardens in consultation. Members were to help each other by counsel and deed. In case of any slander or evil act of one member to another, if proved by three witnesses, the offender was to be fined, make amends to the aggrieved, and apologize.

In all probability, this truce between the two Guilds was short lived. The old jealousies and antagonisms were soon in full play, with each Guild going its own way. This continued until the Uniting Act of 1540. In this year the union of the unincorporated Surgeons' Guild was united with the incorporated Company of Barbers. The Act was passed by Parliament on July 24, 1540, in the thirty-second year of the reign of King Henry VIII, and was the culmination of resentment felt by the public and the civil authorities at the interminable

strife between these two bodies. Both practiced surgery, and, in consequence, "Great contention did arise, and for ty it was most meete and necessary yt the said companyes should be united and made one whole body." The incongruity of the surgeons and barbers uniting is quite puzzling when one considers that, with science advancing, the two crafts, then as now, were dissimilar both in their operations and in the training and intelligence necessary for their practice. However, some insight can be gained into the Act's purpose when it is realized that the provisions definitely state what the surgeons may and may not do and similarly for the barbers; it takes enforcement out of local politics and places it nationally; and it settles the Barber-Surgeons in their corporate capacity for many a long year (see Fig. 1).

The ceremony of this union is pictured in the famous Holbein painting in Barber-Surgeons' Hall in London. This work, considered Holbein's masterpiece, measures ten feet long by six feet high and depicts King Henry VIII handing a charter to Thomas Vicary, the Master of the Barber-Surgeons, with members of the Company and Court kneeling in attendance (see Fig. 2). Sidney Young has an interesting story to tell about the picture's interpretation:

"The picture exhibits a Charter with the Great Seal pendant, and has always been popularly known and described as the 'granting of the Charter to the Barber-Surgeons.' On the other hand, however, the King was but 21 years of age in 1512, and 49 in 1540, which latter age accords with the picture. Moreover, Thomas Vicary, the Master receiving the parchment, as well as Ayleff, Harmon and the others represented were members of the Court in the latter year, but not in 1512. (Henry VIII confirmed the Charter of Henry VII in March 1512.) These considerations are sufficient to demolish the 'Charter' theory, and point to the hypothesis that it is the Union of the Barbers' Company with the Guild of Surgeons . . . which is commemorated."

Of the men portrayed in the picture, some have histories worthy of note. Thomas Vicary was a man of great eminence in his profession, having been surgeon to St. Bartholomew's Hospital, and Sergeant Surgeon to Henry VIII, Edward VI, Mary, and Elizabeth. He was the author of a treatise on anatomy. Several biographies of him have been published. Sir John Ayleff was Master in 1538, and surgeon to King Henry VIII, with whom he was doubtless on terms of friendship, as Henry bequeathed him 100 marks. Ayleff treated Henry for fistula-in-ano and cured him, for which the King, in gratitude, bestowed a great estate upon him. Edmund Harmon was "King's Barber," and to him Henry bequeathed 200 marks. He was one of the attesting witnesses of the King's will. John Penn was the "King's Barber and Groom of the Privy Chamber." Dr. William Butts, one of the King's physicians, probably had the best practice of any man of his time. Dr. John Chambre was physician to, and a great favorite of, Henry. He was a fellow and warden of Merton College, Oxon. He was one of the physicians in attendance on Queen Jane at the birth of Edward VI. He was also in attendance on Anne Boleyn in her confinement with Elizabeth.

It is worthy of note that, notwithstanding the depreciating "Barber" part of the title, the Barber-Surgeons, in the course of their history, had among

them some very able and eminent men. Many were knighted or had positions of wealth and affluence, a number were surgeons to the reigning monarch and his family, some held civic offices as sheriff or alderman, and a few became Lord Mayor of London. On the continent this was equally true. Ambroïse Paré, a rustic, came up from the provinces, became a barber's apprentice and eventually one of the great surgeons of all time. Many other famous surgeons acquired their skill in the shops of the barbers.

Fig. 1.—The Barbers' Guild was granted a coat of arms in 1451 by King Henry VI, described as: "Sable, cheveron between three fleams argent," in ordinary language: a silver cheveron between three lancets upon a black background. The fleams were lancets used to perform venesection. In 1569 the Surgeons were granted a coat of arms by King Henry VIII described as: "A spatter of vert et argent thereon a rose gules crowned Golde." Again in plain English: a red rose surmounted by a gold crown upon a green and silver background. These two designs were placed quartered upon the shield with a red cross between them and granted by Henry VIII as the arms of the united Barber-Surgeons.

As the wealth of the individual members grew, it lent itself to the Guild as a whole, so that all the Craft Guilds acquired Guild Halls of their own and some, through bequest or purchase, possessed property of considerable value: income realty, works of art, furnishings, stored foods, and financial resources through rules of membership obligations. The Guilds were a favorite picking grounds to provide funds for royal extravagances and adventure. As an example, on July 1, 1614, a precept was received to the effect that the King had determined to borrow 100,000 pounds from the City, and that the Barber-Surgeons were assessed 600 pounds toward this loan. They were coolly informed that they could compound this by paying a fine of 30 pounds. Knowing that they would never get back a penny of the 600 pounds if lent, they wisely paid the fine.

Fig. 2.

The Guild Halls were elaborate structures, impressive externally and magnificent internally. Barber-Surgeons' Hall was an example (see Figs. 3-5). There was a Livery Hall for meeting and assembly, Court Room for purposes of its name, kitchen with pantries for food and table service, committee rooms, and at one time an amphitheater and museum where anatomical dissections were demonstrated and specimens exhibited. The city authorities provided the bodies of executed criminals for the dissections. The Hall escaped the Great Fire, and so contains today many delightful antiques, art treasures, portraits of royal donors, and charters granted by successive kings of England. The Guild does

not now possess all the treasures once owned. Many standing cups, bowls of silver and gold plate, and other valuables have disappeared. The Guild had been compelled to melt down its plate and to pawn or sell it. In 1643 an assessment of eight pounds per week for three months towards the King's Army compelled them to dispose of 1,000 ounces of their plate. Their greatest treasure is the Royal Grace Cup and Cover which, fortunately, is still in their possession. This, the gift of King Henry VIII, is of gold and silver, weighs twenty-six

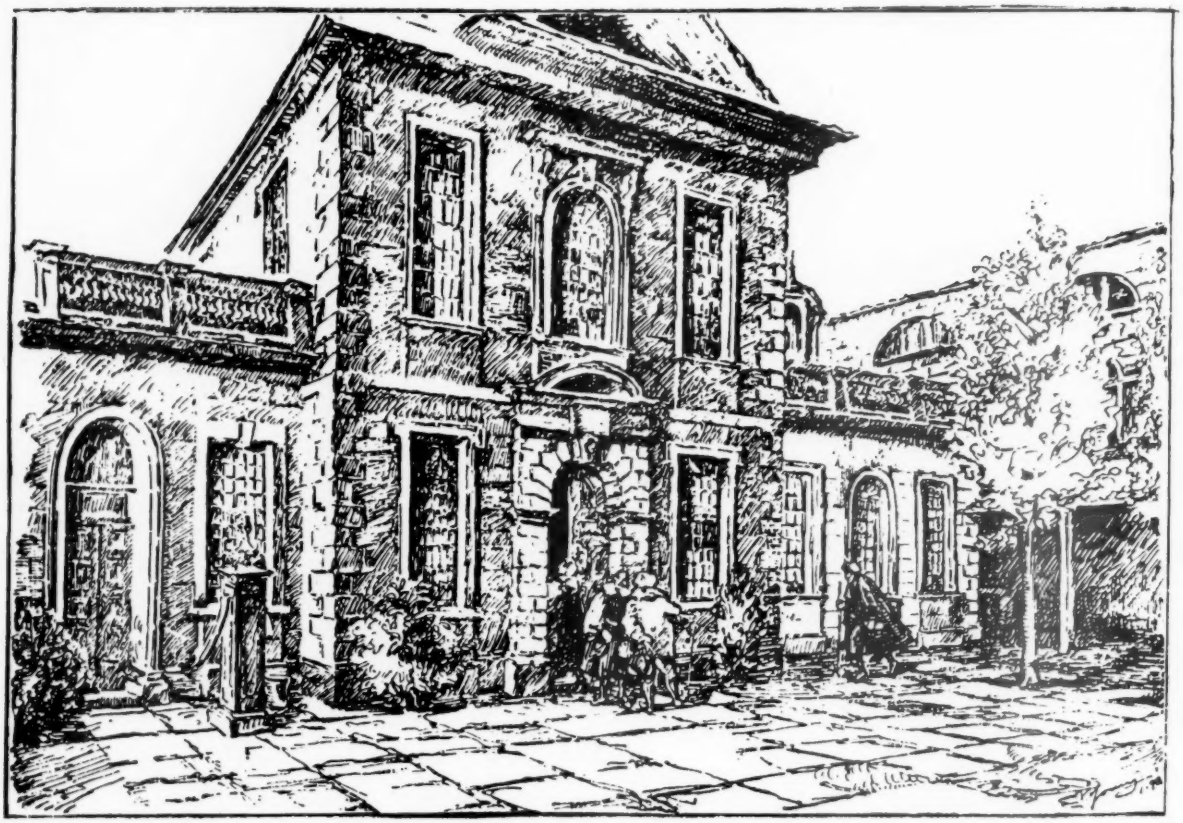

Fig. 3.—Barber-Surgeons' Hall, 1674-1864.

ounces and bears the date 1523. Many experts believe it to be one of the finest pieces of its kind in existence. It is said to have been designed by Holbein and executed by Morett, goldsmith to Henry VIII. An inscription on the cover runs: "Henrici R. munificentia ne Posteris Ignota maneat Johannis Knight, R.C.P., 1678." (R.C.P. stands for Regis Chir. Principal, or Chief Surgeon to the King.) Samuel Pepys dined at Barbers' Hall in 1662 and observes: "Among other observables at the Chyrurgeons' Hall we drank the King's health out of a gift cup given by King Henry VIII to the Company with bells hanging to it which every man is to ring by shaking after he has drunk up the whole cup." The Royal Oak Cup is another important treasure. Presented by Charles II in 1676, it was fashioned in remembrance of the King's escape at Boscobel by hiding in

an oak tree. One old screen of embossed and gilded leather has a remarkable history. It was presented by William Duell, who was hanged at Tyburn. His body was taken to the Hall for dissection where, to everyone's amazement, it was found that he was still alive. He was revived and nursed by the kindly surgeons, and shipped off to the East, where he became a prosperous merchant and presented the screen to the Company in token of his gratitude.

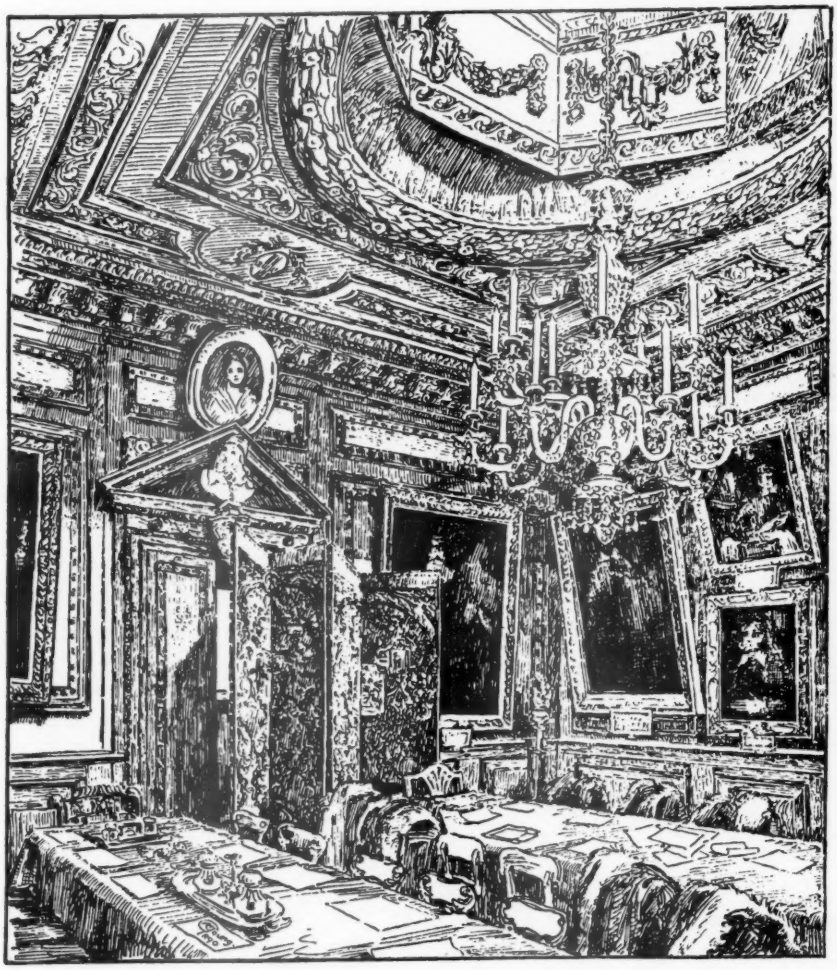

Fig. 4.—Interior of Court Room.

Mention has been made previously of the amphitheater for anatomical demonstrations. These were open to the public and were in charge of the "Masters and Stewards of Anatomy." The Stewards prepared and dissected the body, while the Master gave the lecture. These exhibitions took place four times a year, and were termed "Public Anatomies." The attendance of all the surgeons was compulsory. There were also "Private Anatomies" given to select and invited groups by surgeons having special permission from the Masters. It is one of the Public Anatomies in this theater which Hogarth

satirizes in his ghastly engraving. Besides the dissections, there were lectures on surgery and physic (medicine). The Guild, from the time of its incorporation, endeavored to educate and enlighten its members and apprentices. The exhibits in the museum are smilingly interesting: the skeleton of an ostrich, two human skins on wood frames, of a man and a woman, in imitation of Adam and Eve, a mummy skull, a male skeleton with copper joints, a mummified male with skin and superficial tissues removed to demonstrate muscles, and five other male and female human skeletons.

After each of the Public Anatomies, the Hall was given over to feasting. In fact, food seems to have been a major attraction then as now. The Guild held a monthly dinner, a dinner at elections, and feasts of various magnitude on religious and state holidays. The account book of items for the election dinner of August, 1687, runs as follows:

For a Brace of Bucks	8	13	0
For putting them in 8 Pastyes	4	0	0
For 6 Sr Loynes of Beef and a four rib for brakfast	3	4	0
4 Westfalia hams	1	11	0
7 Lumber pyes	2	16	0
7 Marrow puddings	1	15	0
7 Custarts	1	11	6
7 Dishes of Tarts	2	2	0
7 Dishes of Tonges and Udders	1	15	0
7 Gees	1	5	8
14 Torkeyes	1	11	6
45 Chickens	2	5	0
4 Dozen and ½ Pidgeons	0	13	6
12 Partriges	0	12	0
a Shoulder of Mutton and 2 Rabits for Musick	0	5	0
12 Pounds of midling Bakon and lard	0	8	0
24 Pounds of fresh butter	0	17	0
For Artechoaks Cabidg french beans Lawrell Parsly and herbs to garnish	0	9	0
For Gallidine and Goos Sauce	0	3	6
For viniger	0	6	0
For Brooms packthread Candels and other things	0	1	0
Wood and Coles	1	0	0
Kooks and Laberours and my pains	3	0	0
2 pounds of Loaf Suger	2	0	0
	£40	S6	P8

Next to the feast events, a second great attraction was the numerous processions. For example: to services in St. Paul's on Christmas and Candlemas days, the Lord Mayor's procession, the setting of the watch on Midsummer Eve, the celebration of November fifth, the Anniversary of Gowries Conspiracy, days of thanksgiving, Royal progress, etc., etc. The Liveried members, colorfully gowned, were compelled to go, and often certain of them were ordered to ride horseback, specially adorned in velvet coats with gold chains about their necks. Sometimes the processions were at night and torches were carried. All Guildsmen took part and the apprentices had their place in the line with supervisors to restrain their exuberance.

Membership in a Guild could be secured in three ways: by patrimony, if at the time of an applicant's birth his father was a member; by redemption, by which was meant purchasing or paying for the membership; and by servitude,

which necessitated serving as an apprentice to a member for seven years. This last needs some amplification. The term of servitude was in some instances eight or nine years. The boys were usually taken at the age of 14 years. Before the indentures were sealed, the boy was examined by the Guild Court to determine his physical and mental fitness. If he was approved, the indentures were executed and recorded. In all cases the apprentice lived with his master, who bound himself to furnish food, apparel, lodgings, and all necessaries, according to the custom of the city. If the boy's master died or was unable to continue his business, the boy was turned over to another master, member of the

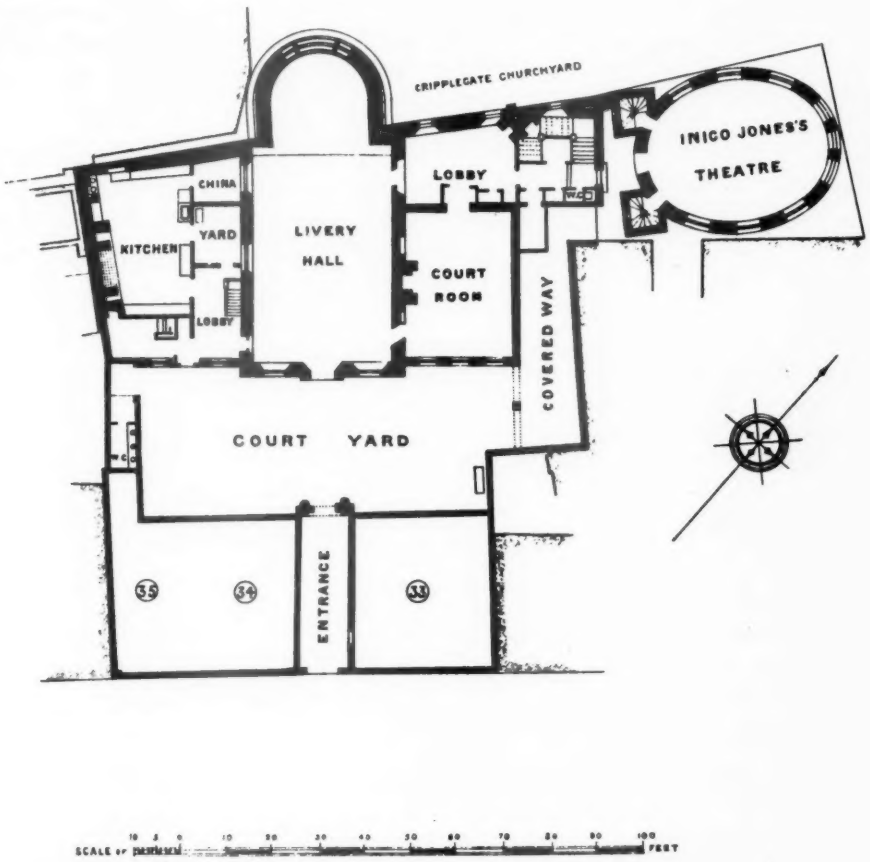

Fig. 5.—Plan of Barber-Surgeons' Hall.

Guild, and the action recorded to prevent the boy's disqualification for his freedom. When his term expired, the master brought him to the Hall and testified to his faithful service, whereupon he became entitled to his freedom upon payment of a nominal fee. Sometimes masters refused to make their apprentices free, in which case the court inquired into the circumstances and acted in accordance with the merits of the case.

The apprentices always seem to have been a source of trouble, both to their masters and to the Guild. Witness some of the entries:

Aug. 22d., 1569. Here was Rich Upton, Playntyf against his apprentice Wm. Fyshe for that he ranne awaye frome his said Master the XXI th of the former month and took with hym s'ten instruments for surgery and other things more . . . said Wm. Fyshe confessed . . . punishment unto auncyent custom with roddes. . . .

Feb. 15th., 1572. Here was Henry Lusshe and witnessed how that his apprentice Rafe Soda ranne away from hym and contract hym self to three women and was asked at Westminster in the Church and who had also delt unhonestly with his mayde servant. . . .

Nov. 3d., 1601. This day upon hearing the controversie betwixt John Howe and his apprentice it was ordered that he shall take home his apprentice and use him well hereafter. . . .

Sept. 27th., 1614. At this Court Ralph Dixon the apprentice of our Master Mr. Hassall for many lewd misdemeanors and for getting a woman with child, being an apprentice should have had the correction of the howse, but upon consideracon had he is to be sent to bridewell.

In the minute books of the Guild Court are numerous entries of a similar character. It is worthy of note that, as correctives for these escapades, the rod was not spared. Juvenile delinquency today could benefit by the example.

The general membership also came in for Court attention. Witness the following:

Oct. 8th., 1577. Here was complainte made by one Mrs. Riche against Robt. Bewsy for that he had her husbone to cure who died and the said Bewsy said and reported that she was an Evell liver and that he died of a botch called Bubo Veneria and taken of her, which he denied, but being proved she put the matter whollie to this Court who did award that he sholde in the presence of her nighbors who were here present in the p'lor upon his knees aske her forgevenes which he did and so the matter was fully ended. . . .

Aug. 13, 1713. Upon hearing a complaint against Mr. Godman and Mr. Pinsent for pretending that one Vincents thigh was broke when it was not and then they had sett it contrary to truth and proficiency in Surgery and the Patient and other witnesses being examined and proving ye fact against him, the Court fined Mr. Godman five pounds for his unskillful and welfull practice and to be sued upon the by law or his bond as shall be thought most convenient.

On January 19th, 1712, Mr. Bartlett, a trussmaker, having been summoned for practicing surgery, was ordered to "take from his sign board that he cured Ruptures."

The above examples are only a few of the many court hearings. The majority of the complaints were for violations of rules and regulations, some being from disgruntled patients. Some of the latter showed both greed and crass malpractice on the part of some Barber-Surgeons. This situation seems puzzling, in view of the Charter provision that surgeons were licensed only after examination by the Masters and Wardens. However, some of the Church and civil dignitaries had authority to grant licenses and did so, for a price, to some pretty poor subjects. The Guild was often helpless in prosecuting these offenders. Then, too, some of the Barber element in the Guild, who were licensed to do only barbering, entered surgical practice and were brought to terms only when discovered.

The incorporation of the barbers and surgeons into one company was never a happy union. The Master of the Guild was, by regulation, chosen alternately from the two groups, one year a barber and the next year a surgeon. The physicians in time were incorporated as the Royal College of Physicians, a decidedly august body. The surgeons were greatly annoyed by the attitude of the physicians, who still treated them as if they were barbers. They were prosecuted if they dared to give "inward physic" to any of their patients. Surgeons who were in the Army and Navy were occasionally captured and though sometimes accorded the honorable position of surgeon, more frequently were treated as barbers. The surgeons accused the Barber-Surgeons' Company, where the barbers were in the majority and had the determining vote, of rushing apprentices through an inadequate servitude, of giving surgical licenses to inadequately prepared candidates from the country, and of limiting the practice of surgery to the city of London. The surgeons felt that they had a better chance of establishing a high standard if they were able to go it alone.

William Cheselden was the most outstanding figure in English surgery during the first half of the eighteenth century. It was due to his efforts and those of his famous pupil, John Hunter, that in 1800 the old Civic Corporation of Surgeons became the Royal College of Surgeons.

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Book Reviews

Review of Modern Trends in Obstetrics & Gynecology. Edited by Kenneth Bowes, London. Pp. 778, with 139 illustrations. New York, 1950, Paul B. Hoeber, Inc. $12.50.

This is the first edition of a volume edited by a noted English gynecologist and obstetrician, in which an attempt has been made to bring together material from various fields closely related to the development of modern obstetrics and gynecology. As mentioned by the editor, the pendulum has swung back from the period in which the majority of advances in obstetrics and gynecology were made by the clinicians only. Now, as the specialty advances, major scientific contributions are being made by specialists in other branches of biology.

In this volume, a thorough coverage of modern developments in obstetrics and gynecology, considered in their broadest aspects, is presented in the form of fifty chapters written by different British clinicians and scientists, together with a few American contributors. It will serve as an excellent text for both student and clinician alike, offering in an easily readable fashion complete information regarding the modern anatomic, endocrinologic, physiologic, sociologic, pathologic, biochemical, clinical, and legal advances in obstetrics and gynecology. Only the most recent advances in antibiotic therapy have been omitted, because the publication of the text unfortunately preceded their development.

The chapters on operative gynecology present mainly the English viewpoint, and this will probably encounter some disagreement from American readers as regards indications for various operations.

However, this text can well be recommended as a worth-while addition to obstetric and gynecologic literature.

Anxiety in Pregnancy and Childbirth. By Henriette R. Klein, M.D., Associate in Psychiatry, Howard Potter, M.D., Professor of Psychology, Long Island College of Medicine, and Ruth B. Dyk, M.S., Research Department, New York City Youth Board, Pp. 111, with few illustrations. New York, 1950, Paul B. Hoeber, Inc. $2.75.

This is the report of a study of twenty-seven primiparous patients who were attending a Brooklyn clinic for prenatal care. They were seen by competent psychiatrists and social workers at frequent intervals both at home and in the prenatal clinic. A detailed psychiatric history of each patient is appended.

The findings are astonishing. Three-quarters of the patients came from homes which had been broken up. The women in the group had few or no intellectual interests, and most of them showed uncertainty or dissatisfaction with their marriages. They had for the most part become pregnant without plan or design, and while there was less rejection of the pregnancy than this might have suggested, most of them were unwilling to nurse their children. Romantic notions and glorification of motherhood were noticeably absent. Physical symptoms during pregnancy were found to be related to the stability of the mother, to whether the child was wanted, and to the degree of success of the marital adjustment.

One gets the impression that these women sense an inescapable and unpleasant fate to which they react without plan. It is hard to believe that this is a common pattern, applicable to other geographic areas of this country in anything like this degree.

The material is not extensive enough to allow conclusions to be drawn.

Genito-Urinary Surgery. By Sir John Thompson-Walker, King's College Hospital, London. Edited and revised by Kenneth Walker. Ed. 3. Pp. 956, with 288 illustrations. New York and London, 1950, Paul B. Hoeber, Inc. $15.00.

The editor intentionally maintains the tenor of the original author's work in this edition. The advances and changes in urology since the second edition (1936) are not adequately covered in the reviewer's opinion. Very few references have been added since 1936. Conservative renal surgery, transurethral procedures, and the role of the newer antibiotics have insufficient coverage.

The chapters on echinococcosis and schistosomiasis are excellent. Coverage of "office urology" is quite adequate but, in part, outmoded.

Pathology in General Surgery. By Paul W. Schaffer, M.D., University of Kansas School of Medicine, Kansas City, Kansas. Pp. 581, with many illustrations. Chicago, 1950, University of Chicago Press. $17.50.

Dr. Schaffer has gathered together in this text the finest collection of reproductions of gross and microscopic pathology to be published in one volume. Presented essentially for the clinician, the vivid illustrations portray disease processes with unmatched realism. The text is brief and lucid and essentially highlights the pathologic process brought out by the strikingly reproduced specimens. Each discussion is followed by a useful bibliography. Although not a complete textbook of pathology, this volume gives to its reader a lifelike museum of pathologic material, well-preserved, indexed, classified, and described. As a supplement to more orthodox texts of pathology this publication will be widely used by surgeons, practitioners, internists, and radiologists, as well as teachers and students. It is a gem to adorn every surgeon's library.

Tumors of the Head and Neck. By Grant E. Ward, M.D., F.A.C.S., and James W. Hendrick, M.D., M.S., Department of Surgery, School of Medicine, University of Maryland. Pp. 832, with many illustrations. Baltimore, 1950, Williams and Wilkins Company, $15.00.

The long existing need for a good text on treatment of tumors of the head and neck area has been very amply met by this authoritative publication by Ward and Hendrick. The book is well organized and comprehensive in its scope. It develops each problem from its pathologic to its clinical aspects, stresses the importance of early diagnosis, and presents the problem of therapy in detail from the point of view of the surgeon as well as of the radiotherapist. Each method of treatment is fairly appraised and described, so that it complements another method when necessary. The bibliography is complete and useful, and in addition, the authors present much of their vast and long personal experience in treating tumors in this area. The ample illustrations are well reproduced and carefully chosen to enrich the presentation. All specialists with an interest in tumors in this area, as well as general practitioners and students, will find much useful and practical information in this excellent publication.

Menstruation and Its Disorders. Proceedings of the Conference held under the Auspices of the National Committee on Maternal Health, Edited by Earl T. Engle. Pp. 358. Springfield, Ill., 1950, Charles C Thomas, Publisher. $6.50.

The title of this volume is misleading. It contains the papers presented before a conference held under the auspices of the National Committee on Maternal Health. Each paper is a summary of the results of the study of a small, complicated part of the large field of endometrial function, and many of the findings are so new that conclusions cannot be drawn. Limitations of space make it impossible to review the papers adequately.

There are four papers dealing with some enzymes of the endometrium and ovary by W. B. Atkinson, George B. Wislocki, et al., George Gomori, and R. K. Meyer. Hertig and Rock have briefly summarized their findings on very early implanted human eggs. Harold Okkels of Copenhagen, and J. E. Markee present their studies on endometrial blood vessels and some problems of endometrial blood flow. Olive and George Van S. Smith present their data on the experimental and clinical studies related to their so-called menstrual toxin. Ephraim Shorr discusses peripheral vascular homeostasis. Te Linde discusses briefly some aspects of the histology of functional uterine bleeding, and C. L. Buxton adds to this in a discussion of the atypical secretory phase. The final paper is a report of studies of the use of intrauterine electrodes in recording uterine muscle function.

These papers not only present the work of the authors, but point out the direction of interest and work which is likely to be followed in the future. They contain fascinating suggestions and information which must be read in the original to be appreciated.

Die Frühdiagnose des Uteruscarcinoms (The Early Diagnosis of Carcinoma of the Uterus). By Hans Limberg, Prof. Dr. Med. Universitats Frauenlklinik, Hamburg. Pp. 158, with 75 illustrations. Stuttgart, 1950, Georg Thieme verlag.* New York, Grune & Stratton, Inc. $3.50.

This volume is made up of 120 pages of text which is followed by 38 pages of nicely reproduced photomicrographs. It is written in German and is designed to bring to the attention of German workers the information on the smear diagnosis of gynecologic malignant disease which has been obtained elsewhere during and since World War II. The references are very complete and adequately summarized. The author has repeated in Hamburg a considerable part of the studies which have been done elsewhere, and has produced similar results.

There is nothing new in this volume except what may be an interesting staining technique for vaginal smears. Interestingly enough, the volume is dedicated to Robert Meyer.

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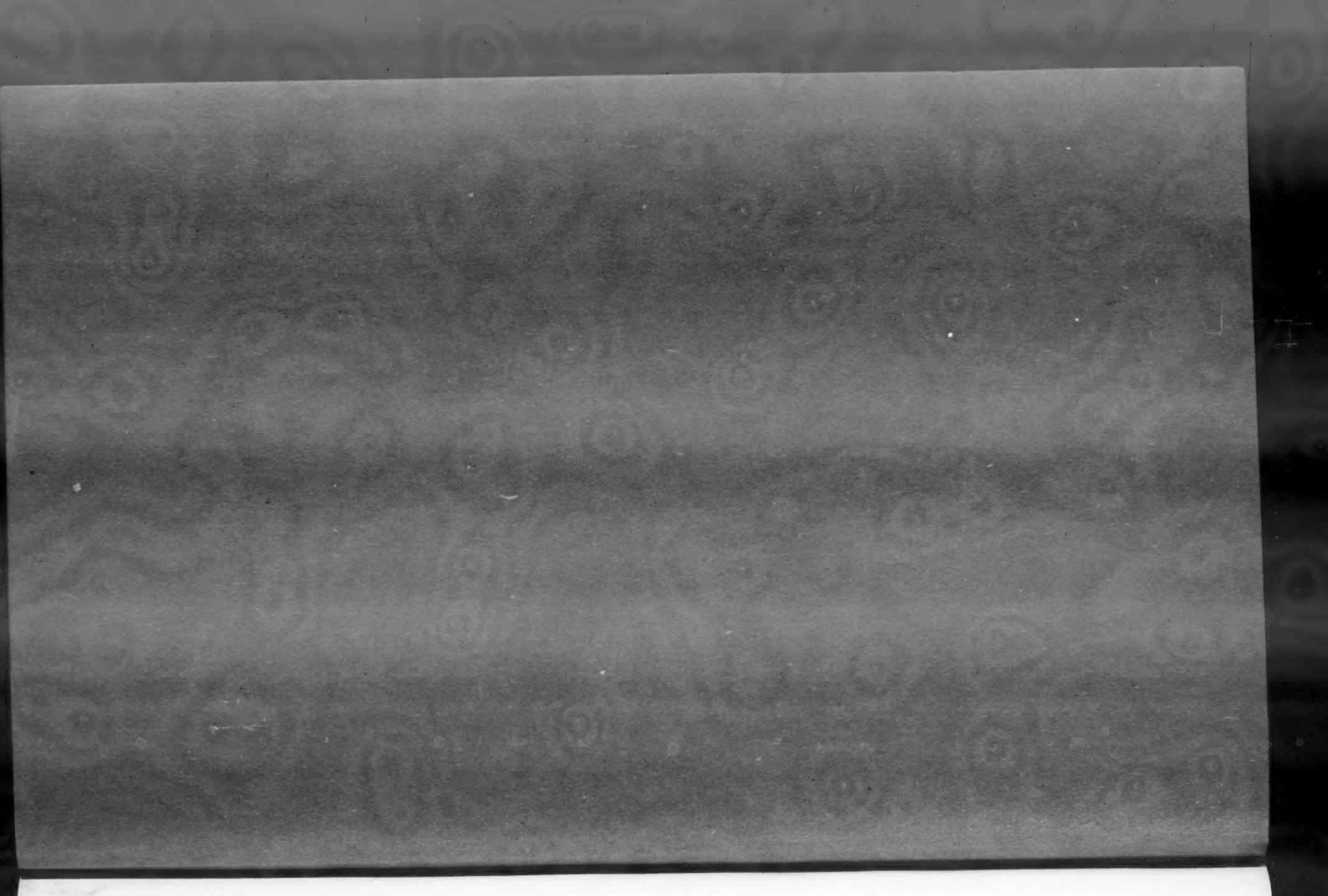
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